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Proposed Registration Decision PRD2014-21

Momfluorothrin

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Overview

Proposed Registration Decision for Momfluorothrin

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Momfluorothrin Technical Grade, as well as three manufacturing concentrates: Sumifreeze Manufacturing Use Product, MGK 2983 and MGK 2987; and four domestic class end-use products: Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 29831, MGK 29871 and MGK 29872. All four end-use products are used to control a variety of insect and spider species found indoors and outdoors at residential locations. The end-use products are also coformulated with either d-phenothrin or piperonyl butoxide.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of momfluorothrin and its associated manufacturing concentrates and end-use products (Sumifreeze Manufacturing Use Product, MGK 2983, MGK 2987, Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 29831, MGK 29871 and MGK 29872).

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on momfluorothrin, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on momfluorothrin, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Momfluorothrin?

Momfluorothrin is a new pyrethroid insecticide that kills insects and spiders on contact. It may be used indoors and outdoors at residential locations. It rapidly immobilizes most pests after treatment which may reduce the distance the target pest travels after treatment. This may allow easier disposal of dead insects and spiders.

Health Considerations

Can Approved Uses of Momfluorothrin Affect Human Health?

Products containing momfluorothrin are unlikely to affect your health when used according to label directions.

Potential exposure to momfluorothrin may occur when handling and applying end-use products containing momfluorothrin. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

In laboratory animals, the technical grade active ingredient momfluorothrin was of high acute toxicity by the oral route; consequently, the signal word and hazard statement "DANGER–POISON" are required on the label. It was of low acute toxicity dermally and through inhalation exposure. Momfluorothrin was minimally-irritating to the eyes and non-irritating to the skin, and did not cause an allergic skin reaction.

There are three manufacturing concentrates (Sumifreeze Manufacturing Use Product, MGK 2987 and MGK 2983) containing momfluorothrin. Sumifreeze Manufacturing Use Product was of low acute toxicity via the oral and dermal route of exposure, but was slightly toxic via the inhalation route. It was non-irritating to the skin, but mildly irritating to the eyes, and did not cause an allergic skin reaction. Based on these findings, the signal word and hazard statements "CAUTION-POISON" and "EYE IRRITANT" are required on the product label.

MGK 2987 was of moderate acute toxicity via the oral route of exposure, was slightly toxic via the inhalation route, and was of low toxicity via the dermal route. It was mildly irritating to the skin and eyes, but did not cause an allergic skin reaction. Based on these findings the signal word and hazard statements "WARNING-POISON" and "EYE AND SKIN IRRITANT" are required on the product label.

MGK 2983 was of moderate acute toxicity via the oral route of exposure, but was of low acute toxicity via the dermal and inhalation routes. It was non-irritating to the skin and eyes, but produced an allergic skin reaction. Consequently, the signal word and hazard statements "WARNING-POISON" and "POTENTIAL SKIN SENSITIZER" are required on the product label.

There are four end-use products (Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 29831, MGK 29871, MGK 29872) containing momfluorothrin.

Momfluorothrin Flying and Crawling Insect Killer Spray was of low acute toxicity via the oral and dermal routes of exposure, and was of slight toxicity via the inhalation route. Consequently the signal word and hazard statement "CAUTION-POISON" are required on the label. It was minimally irritating to the skin, not irritating to the eyes and did not cause an allergic skin reaction.

MGK 29831 was of low acute toxicity via the oral, dermal, and inhalation routes of exposure. It was minimally irritating to the skin and eyes and produced an allergic skin reaction. Consequently, the hazard statement "POTENTIAL SKIN SENSITIZER" is required on the product label.

MGK 29871 was of low acute toxicity via the oral, dermal, and inhalation routes of exposure. It was not irritating to the skin and eyes and did not cause an allergic skin reaction.

MGK 29872 was of low acute toxicity via the oral, dermal, and inhalation routes of exposure. It was minimally irritating to the skin and eyes and did not cause an allergic skin reaction.

Health effects in animals given repeated doses of momfluorothrin primarily involved effects on the liver and nervous system. There was no indication that momfluorothrin caused damage to the immune system. Momfluorothrin did not cause birth defects in animals and there were no effects on the ability to reproduce. There was no evidence to suggest that momfluorothrin damaged genetic material. Momfluorothrin did, however, cause liver tumours in rats following prolonged dosing.

When momfluorothrin was given to pregnant or nursing animals, decreased body and spleen weights were observed in the juvenile animal at doses that were not toxic to the mother, suggesting that the young may be more sensitive to momfluorothrin than the adult animal.

The risk assessment protects against the effects of momfluorothrin by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Risks in Residential and Other Non-Occupational Environments

Estimated risk for residential exposure is not of concern provided that directions specified on the label are observed.

Residential exposure to adults applying momfluorothrin and contacting treated surfaces is not expected to result in unacceptable risk when momfluorothrin is used according to label directions. Exposure to youth (11 < 16 years) and children (1 < 2 years) contacting treated surfaces is not of concern when momfluorothrin is used according to label directions.

Occupational Risks From Handling Momfluorothrin

The momfluorothrin products are domestic class end-use products so exposure to occupational users is not of concern.

Environmental Considerations

What Happens When Momfluorothrin Is Introduced Into the Environment?

Momfluorothrin will not persist in soil and water. As the environmental exposure to momfluorothrin will be very limited if used according to the proposed label, the risk to organisms in the environment is negligible.

Products containing momfluorothrin are proposed to be used as a crack and crevice or spot treatment (only) indoors and outdoors to control flying and crawling insects. Insects are controlled by direct contact with the insecticide when it is sprayed from an aerosol can. These products may be used to control insects outside at residential locations. The contents of insect nests are not to be treated with these products. Low environmental exposure from momfluorothrin is expected from these uses as a household aerosol spray because only small, limited areas are being treated where insect pests are visible. If momfluorothrin enters the environment, it will break down quickly in soil and water by microorganisms. Break down of

momfluorothrin in water in the presence of light will be limited. Momfluorothrin binds strongly to soil and is unlikely to bioaccumulate in fish.

Momfluorothrin is practically non-toxic to terrestrial organisms that were studied, but is highly toxic to honeybees when they are directly contacted with the insecticide spray. This chemical is also very highly toxic to aquatic organisms, such as fish and aquatic invertebrates. Considering that momfluorothrin is proposed as a household aerosol spray, the potential for exposure of non-target terrestrial and aquatic organisms in the environment is expected to be very limited. Therefore, risk to non-target organisms is also expected to be minimal.

Value Considerations

What Is the Value of Momfluorothrin Flying and Crawling Insect Killer Spray?

Momfluorothrin Flying and Crawling Insect Killer Spray kills ants, cockroaches, several fly species, several stinging insect species and spiders found indoors and outdoors at residential locations.

Momfluorothrin Flying and Crawling Insect Killer Spray is a ready-to-use spray that combines momfluorothrin with another pyrethroid, d-phenothrin. The combination of these two active ingredients demonstrated improved efficacy against insects and spiders compared to either active ingredient alone.

What Is the Value of MGK 29831?

MGK 29831 kills several fly and moth species found indoors and outdoors at residential locations.

MGK 29831 is a ready-to-use spray that combines momfluorothrin with a synergist, piperonyl butoxide. The addition of piperonyl butoxide increased the efficacy of momfluorothrin against house flies compared to momfluorothrin alone.

What Is the Value of MGK 29871 and MGK 29872?

MGK 29871 and MGK 29872 kill several stinging insect species found indoors and outdoors at residential locations.

MGK 29871 and MGK 29872 are ready-to-use sprays that combine momfluorothrin with another pyrethroid, d-phenothrin. The combination of these two active ingredients demonstrated improved efficacy against insect pests compared to either active ingredient alone.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 29831, MGK 29871 and MGK 29872 to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

To avoid direct contact with momfluorothrin on the skin, by inhalation, or through incidental-oral ingestion, follow the label directions.

Environment

Hazard label statements are required to inform users that these products are toxic to aquatic organisms and bees.

Label statements also limit the outdoor use of momfluorothrin-containing products to crack and crevice or spot treatments, and indicate no direct application to water is allowed.

Next Steps

Before making a final registration decision on momfluorothrin, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

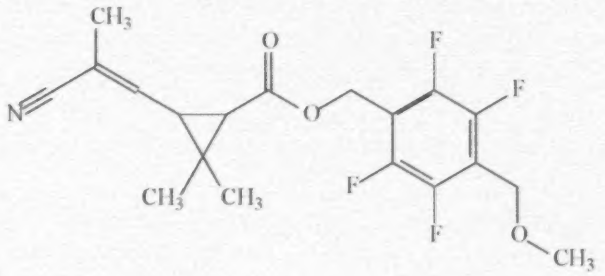
When the PMRA makes its registration decision, it will publish a Registration Decision on momfluorothrin (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Momfluorothrin

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Momfluorothrin
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (EZ)-(1RS,3RS;1RS,3SR)-3-(2-cyanoprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate
2. Chemical Abstracts Service (CAS)	[2,3,5,6-tetrafluoro-4-(methoxymethyl)phenyl]methyl 3-(2-cyano-1-propen-1-yl)-2,2-dimethylcyclopropanecarboxylate
CAS number	609346-29-4
Molecular formula	$C_{19}H_{19}F_4NO_3$
Molecular weight	385.35
Structural formula	
Purity of the active ingredient	96.16%

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

Technical Product—Momfluorothrin Technical Grade

Property	Result
Colour and physical state	Pale yellow crystalline solid
Odour	No odour detected
Melting range	65.95–73.30°C
Boiling point or range	N/A

Property	Result
Specific gravity	1.366
Vapour pressure at 20°C	2.478×10^{-7} Pa
Henry's law constant at 20°C	1.024×10^{-4} Pa m^3 mol^{-1}
Ultraviolet (UV)-visible spectrum	Absorbance maxima: Acidic conditions: 218.80 nm, ε = 22717.50 271.86 nm, ε = 1863.56 Neutral conditions: 218.73 nm, ε = 22003.18 271.84 nm, ε = 1774.12 Basic conditions: 218.38 nm, ε = 17440.56 234.40 nm, ε = 14865.32
Solubility in water at 20°C	0.933 ± 0.0916 mg/L at 20°C (double-distilled water)
Solubility in organic solvents at 20°C	Solubility at 20°C (g/L) n-Heptane: < 10 n-Octanol: < 10 Acetone: > 250 1,2-Dichloroethane: > 250 Ethyl acetate: > 250 p-Xylene: > 250 Methanol: 67-80
n-Octanol-water partition coefficient (K_{ow})	Log K_{ow} = 2.99 at 25°C
Dissociation constant (pK_a)	The structure contains no groups with appreciable acidic or basic characters. The active will be unionized in the environmental pH range.
Stability (temperature, metal)	Stable when stored at 53–56°C for 14 days.

Manufacturing Concentrate and End-Use Products

Property	Sumifreeze Manufacturing Use Product	Momfluorothrin Flying and Crawling Insect Killer Spray
Colour	Yellow	White
Odour	No odour	No odour
Physical state	Transparent liquid	Opaque emulsion
Formulation type	Liquid	Pressurized product
Guarantee	Momfluorothrin 15.7%	Momfluorothrin 0.10% d-Phenothrin 0.20%
Container material and description	Metal drum, 20 kg	Steel aerosol can with press-button actuator, 200 g
Specific gravity	1.207 – 1.208	0.967
pH of 1% dispersion in water	6.02	5.8
Oxidizing or reducing action	N/A	N/A

Property	Sumifreeze Manufacturing Use Product	Momfluorothrin Flying and Crawling Insect Killer Spray
Storage stability	Stable when stored for one year at ambient temperature in commercial packaging.	Stable when stored for 12 months at 25±2°C in commercial aerosol containers.
Corrosion characteristics	Not corrosive to the container material.	Not corrosive to the container material.
Explodability	Not explosive	Not explosive

Property	MGK 2983	MGK 29831
Colour	Light amber	Creamy white
Odour	Sweet surfactant odour	Slight surfactant odour
Physical state	Liquid	Oil
Formulation type	Solution	Pressurized product
Guarantee	Momfluorothrin 2.225% Piperonyl butoxide 17.2%	Momfluorothrin 0.05% Piperonyl butoxide 0.39%
Container material and description	Metal steel drum 15 L to 250 L	Metal aerosol can 50 mL to 750 mL
Density	0.997 g/cm^3	0.968 g/cm^3
pH of 5% dispersion in water	5.6	5.9
Oxidizing or reducing action	Does not contain any oxidising or reducing agent.	Does not contain any oxidising or reducing agent.
Storage stability	Stable when stored for 12 months at room temperature in amber glass and FL-HDPE	Stable when stored for 12 months at room temperature in lined aerosol containers.
Corrosion characteristics	Not corrosive to amber glass or fluorinated HDPE containers1	Not corrosive to the container material.
Explodability	Not considered to be potentially explosive.	Not considered to be potentially explosive.

Property	MGK 2987	MGK 29871	MGK 29872
Colour	Pale yellow	Opaque	Colourless
Odour	Sharp sweet odour	Sweet odour	Sharp sweet odour
Physical state	Liquid	Liquid	Liquid
Formulation type	Solution	Pressurized product	Pressurized product
Guarantee	Momfluorothrin 5.00% d-Phenothrin 20.00%	Momfluorothrin 0.050% d-Phenothrin 0.200%	Momfluorothrin 0.050% d-Phenothrin 0.200%
Container material and description	Metal steel drum 15 L to 250L	Metal aerosol can 50 mL to 750 mL	Metal aerosol can 50 mL to 750 mL
Density	1.008 g/cm^3	0.996 g/cm^3	0.788 g/cm^3
pH of 5% dispersion in water	6.0	6.5	5.25 (1% aqueous dilution)
Oxidizing or reducing action	Does not contain any oxidising or reducing agent.	Does not contain any oxidising or reducing agent.	Does not contain any oxidising or reducing agent.

Property	MGK 2987	MGK 29871	MGK 29872
Storage stability	Stable when stored for 12 months at room temperature in amber glass and FL-HDPE.	Stable when stored for 12 months at room temperature in lined aerosol (DS) containers.	Stable when stored for 12 months at room temperature in lined aerosol (DS) containers.
Corrosion characteristics	Not corrosive to amber glass or fluorinated HDPE containers	May be slightly corrosive to the container material. Not expected to have any effect on the service lifetime of the container.	Not corrosive to the container material
Explodability	Not considered to be potentially explosive.	Not considered to be potentially explosive.	Not considered to be potentially explosive.

1.3 Directions for Use

Momofluorothrin Flying and Crawling Insect Killer Spray:
Momfluorothrin Flying and Crawling Insect Killer Spray is a ready-to-use spray that may be applied both indoors and outdoors at residential locations. It is applied either as a crack and crevice or spot treatment to kill ants, cockroaches, house flies, hornets, mosquitoes, paper wasps, spiders, stable flies and yellow jackets on contact.

MGK 29831:
MGK 29831 is a ready-to-use spray that may be applied both indoors and outdoors at residential locations. It is applied either as a crack and crevice or spot treatment to kill Angoumois grain moths, clothes moths, fruit flies, house flies, horn flies, Indian meal moths, lesser house flies, Mediterranean flour moths, mosquitoes and stable flies on contact.

MGK 29871 and MGK 29872:
MGK 29871 and MGK 29872 are ready-to-use sprays that may be applied both indoors and outdoors at residential locations. They are applied either as a crack and crevice or spot treatments to kill wasps, hornets and yellow jackets on contact.

1.4 Mode of Action

Momfluorothrin is a pyrethroid belonging to mode of action-group 3. It kills insects and spiders by interfering with the sodium channels of nerves.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and impurities in the technical product have been validated and assessed to be acceptable for the determinations.

2.2 Methods for Formulations Analysis

The methods provided for the analysis of the active ingredients in the formulations have been validated and assessed to be acceptable for use as enforcement analytical methods.

2.3 Methods for Residue Analysis

A gas chromatography method with tandem mass spectrometry (GC-MS/MS) was developed and proposed for data generation and enforcement purposes. This method fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (90 - 91%) were obtained in environmental media. The method for residue analysis is summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Momfluorothrin is a Type I synthetic pyrethroid insecticide comprised of eight individual isomers. Synthetic pyrethroids induce neurotoxic effects primarily by binding to voltage-dependant sodium channels in neurons, thereby delaying the closing of the sodium channels and causing the depolarization of neurons. This affects action potentials and results in either repetitive activity (Type I pyrethroids) or blockage of nerve conduction (Type II pyrethroids). Type I pyrethroids such as momfluorothrin induce a syndrome in rats consisting of aggressive sparring, altered sensitivity to external stimuli, and fine tremors progressing to whole-body tremor and prostration (T-syndrome).

A detailed review of the toxicological database for momfluorothrin was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to momfluorothrin.

Toxicokinetic data for momfluorothrin are based on studies in which rats were administered single low or high doses of the radiolabelled Z- or E isomer, or repeated low doses of the Z-isomer. Radiolabelled momfluorothrin was extensively absorbed (estimated to be 90% and 80% of the administered dose for the Z- and E-isomers, respectively), based on the amounts of radioactivity excreted into the bile and urine. Maximum plasma concentrations occurred within 4-8 hours following low dose administration of both isomers, and following high dose administration of the E-isomer. Peak plasma concentrations were not reached until 12 hours following administration of the higher dose of the Z-isomer. Slight sex-related differences were observed, with higher plasma concentrations being reached in females at both doses, and for both isomers.

Distribution in organs and tissues was similar following a single low or high dose of either isomer. Tissue concentrations were generally low, but highest levels were found in the liver, kidney and gastrointestinal tract. Momfluorothrin was metabolized primarily through cleavage of the ester linkage, leading to conjugation with glucuronic acid and isomerization of the glucuronide. Major metabolites in the urine included Z-CMCA, ωHM-CMCAZ, and 2CHM-CMCAZ (also known as M4). Elimination was rapid and for the Z-isomer occurred primarily via the feces in males and the urine in females. The urine was the major route of elimination for the E-isomer in both sexes. Elimination of momfluorothrin tended to be slower in males. Biliary excretion accounted for approximately 45-60% of the administrated dose, depending on the isomer. The excretion pattern was not altered by repeated-dose administration.

Technical momfluorothrin was of high acute toxicity in rats via the oral route of exposure. It was of low acute toxicity in rats via the dermal and inhalation routes. It was minimally irritating to the eyes, but non-irritating to the skin of rabbits, and was not a potential skin sensitizer when tested in guinea pigs using the Maximization method.

Sumifreeze Manufacturing Use Product, MGK 2987, and MGK 2983 are manufacturing concentrates that contain momfluorothrin. Two of these products (MGK 2987, MGK 2983) were moderately acutely toxic to rats via the oral route of exposure, and the other was of low acute toxicity via this route. Two products (Sumifreeze Manufacturing Use Product, MGK 2987) were slightly acutely toxic to rats via inhalation, while MGK 2983 was of low acute toxicity. All were of low acute toxicity to rats via the dermal route of exposure and were non-irritating to mildly irritating to the eyes and skin of rabbits. MGK 2983 induced a positive sensitization response in mice.

Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 29871, MGK 29872, and MGK 29831 are end-use products that contain momfluorothrin. These four products were considered to be of low acute toxicity in rats via the oral and dermal routes of exposure. Momfluorothrin Flying and Crawling Insect Killer Spray was slightly acutely toxic via inhalation exposure, whereas the other three products were of low acute toxicity via this route. All products were non-irritating or minimally irritating to the eyes and skin of rabbits. MGK 29831 was considered to be a dermal sensitizer; however, the other three were negative.

Repeat-dose oral studies conducted with momfluorothrin in mice and rats via dietary administration and dogs via capsule administration revealed that the liver was a target organ of toxicity. Increased liver weight was noted at the lower dose levels, whereas histopathological changes including hepatocellular hypertrophy, was observed at higher dose levels. Single-cell necrosis of hepatocyte was observed at the highest dose level in the 78-week mouse study. Decreased body weights compared to controls were consistently noted throughout the database following dietary exposure. Alterations in various blood parameters were also observed in rats following dietary exposure. Neurotoxic effects consistent with Type-1 pyrethroids (tremors) were observed in rats following oral gavage dosing, but not dietary exposure. There was some indication of recovery from the toxic effects of momfluorothrin exposure in rats and dogs that were given a 6-week recovery period.

Effects in rats following short-term inhalation exposure were consistent with those observed after oral dosing, namely increases in liver weight and clinical signs of neurotoxicity (tremors). In a short-term dermal toxicity study in rats which included detailed clinical observations in the home cage, hand and open field, no signs of toxicity were noted up to the limit dose of 1000 mg/kg bw/day.

A battery of genotoxicity studies was submitted for momfluorothrin. With the exception of a marginal increase in aberrant cells in an in vitro chromosomal aberration assay using Chinese hamster lung cells, the overall weight of evidence for momfluorothrin did not suggest genotoxic potential. No increase in tumour incidence was observed in a 78-week dietary carcinogenicity study in mice. In a two-year dietary carcinogenicity study in rats, an increased incidence of liver tumours (hepatocellular adenomas, carcinomas, and adenomas/carcinomas combined) was observed in males at the mid- and high dose levels, and in females at the high dose level. The increases were statistically significant at the high dose level in both sexes. A mode of action (MOA) similar to that of phenobarbital was proposed for tumour induction. A description of key events, with dose and temporal relationship was presented and several mechanistic studies to support the MOA were provided. The proposed MOA consisted of activation of the constitutive androstane receptor (CAR), resulting in induction of cytochrome P450 CYP2B enzymes, leading to liver hypertrophy and increased cell proliferation, ultimately resulting in the formation of altered hepatic foci and liver tumours. The proposed MOA was deemed plausible in rodents; however, there were some limitations regarding dose concordance, specifically lack of clear induction of CYP2B enzymes or an increase in altered hepatocellular foci noted at the tumour threshold for males and a lack of smooth endoplasmic reticulum (SER) proliferation noted in both sexes at the highest dose level following 7 days of treatment. Despite these limitations, the overall weight of evidence for the MOA was sufficient to conclude that a linear low dose extrapolation (q_1*) approach to the cancer risk assessment may be overly conservative. For these reasons, a threshold approach for liver tumours was applied for the cancer risk assessment.

Based on the results of the available studies, the rat appeared to be more sensitive than the mouse or dog to the toxicity of momfluorothrin. There was no pronounced evidence of increased toxicity over the short- to intermediate-term duration of dosing. However, there was some evidence of increased toxicity with prolonged duration of oral dosing in rats. This was supported by the appearance of histopathological changes in the thyroid (thyroid follicular cell hypertrophy) in male rats following only long-term oral dosing, as well as the observation of hepatocellular hypertrophy in the 52-week dietary rat study at a lower dose level compared to the 13-week dietary rat study.

In oral gavage developmental toxicity studies in rats and rabbits, no adverse effects were observed in developing fetuses. In rats, clinical signs of neurotoxicity consistent with pyrethroid toxicity were observed in the dams, as evidenced by tremors two to three hours after dose administration between gestation days 15 and 19. No maternal toxicity was noted in rabbits up to the limit dose of testing. The results of these studies provided no evidence of teratogenicity and did not suggest that the young animal was more sensitive than the adult animal to the toxic effects of momfluorothrin.

In a two-generation reproduction study in rats administered momfluorothrin via the diet, there were no adverse effects on measured reproductive parameters. The only effect observed in maternal animals was an increase in liver weight at the highest dose tested, a dose level at which this same finding, as well as liver histopathology and decreases in body weight, were observed in male parental animals. In offspring, decreased bodyweights on post-natal day (PND) 21 and decreased spleen weights were observed beginning at the mid-dose. At the highest dose level, delayed vaginal opening (three days) was observed in offspring and was considered to be related to treatment. The decreased bodyweights and spleen weights that were observed in offspring at a dose level that did not elicit any maternal toxicity suggests that the young animal may be more sensitive than the adult animal to the effects of momfluorothrin exposure. However, these effects were observed during a time period when the young animal would have begun to consume the diet in addition to potentially receiving the test material via the mother's milk. As such, offspring may have received a higher systemic dose of momfluorothrin than the adult animal. In addition, the fact that the reduced spleen weights were not manifested in these animals as adults, as well as the lack of adverse pathology of the spleen, suggests that the findings in offspring were transient. Given the above, there is a low level of concern for the offspring findings that occurred in the absence of toxicity in the adult animal.

Acute and repeated-dose neurotoxicity testing were performed with momfluorothrin in rats. Clinical signs of neurotoxicity, which included increased salivation, straub tail, tremors, twitch and miosis, were observed in the acute studies which employed gavage dosing, but not in the 13-week study in which the test material was administered via the diet. Additionally, tremors were observed in rats in an in vivo bone marrow micronucleus study in which animals received a single oral gavage dose of momfluorothrin.

Despite a lack of significant evidence of increased sensitivity of the offspring in the submitted studies, residual uncertainty remains regarding susceptibility of the young. Literature studies indicate that pharmacodynamic and pharmacokinetic factors, notably age-dependent maturation of key metabolic processes, may lead to increased susceptibility of the young to pyrethroid toxicity. Young animals have incomplete maturation of the enzyme systems that detoxify pyrethroids, particularly the carboxylesterases and cytochrome P450s. Consequently, pyrethroid concentrations in target tissues (for example, brain) may be higher in young animals than in adults given the same dose. In general, pyrethroid neurotoxicity is correlated to peak concentrations of the compound, with gavage dosing patterns resulting in greater internal doses compared to dietary administration. The pyrethroids are regarded as having a narrow window of time-to-peak-effect. The design of a developmental neurotoxicity study does not consider time-to-peak-effect and may miss the window of peak toxicity for the pyrethroids (Scollon, 2010). Accordingly a developmental neurotoxicity study is not required for momfluorothrin. A comparative oral gavage neurotoxicity study conducted in pups, weanlings and adults, which considers the time of peak effect, could address this uncertainty. In the interim, this uncertainty has been reflected in the form of a database uncertainty factor.

In a dietary immunotoxicity study in rats, there was no indication of immunotoxicity.

Results of the toxicology studies conducted on laboratory animals with momfluorothrin and its associated end-use products are summarized in Appendix I, Tables 2(a-g) and 3. The toxicology endpoints for use in the human health risk assessment are summarized in Appendix I, Table 4.

Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA. Information on the reporting of incidents can be found on the Pesticides and Pest Management portion of Health Canada's website. As of May, 2014, there were no incidents of adverse health outcomes reported for momfluorothrin, nor were any additional data pertaining to adverse health effects submitted by the applicant.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the standard complement of required studies was available, including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats.

With respect to potential pre-natal toxicity, there was no indication of increased susceptibility of fetuses compared to parental animals in the oral gavage developmental toxicity studies in rats and rabbits. With respect to post-natal toxicity, in the 2-generation dietary rat reproductive toxicity study, vaginal opening was delayed in the offspring at the highest dose tested, a dose level that only resulted in increased liver weight in maternal animals. Decreased bodyweights on PND 21 and decreased spleen weights were observed in offspring at a dose level that did not elicit any effects in dams, suggesting that the young animal may be more sensitive than the adult animal to momfluorothrin. However, as noted in Section 3.1, these effects occurred during a time period when offspring were likely receiving a higher systemic dose of momfluorothrin than the adult animal (in other words, via the diet and through lactation). Additionally, reduced spleen weight was not manifested in these animals as adults, nor was there any pathology of the spleen observed, which suggests that the findings in offspring were transient. Given the above, there is a low level of concern for the reductions in pup spleen weights occurring in the absence of toxicity in the maternal animal.

Young animals have incomplete maturation of enzyme systems which detoxify pyrethroids and thus may be more susceptible due to higher and prolonged brain concentrations, compared to adults (Kim *et al.*, 2009). Due to the lack of a comparative oral neurotoxicity study, an adequate assessment of sensitivity of the young is currently not available and residual uncertainty remains concerning susceptibility of the young to potential neurotoxic effects. This concern was reflected through the use of a database uncertainty factor of 3-fold in the risk assessment. Since these concerns were addressed with a database uncertainty factor, the *Pest Control Products Act* factor was reduced to 1-fold.

3.2 Acute Reference Dose (ARfD)

Establishment of an acute reference dose (ARfD) is not required as there are no proposed food uses and contamination of drinking water sources is not expected.

3.3 Acceptable Daily Intake (ADI)

Establishment of an acceptable daily intake (ADI) is not required as there are no proposed food uses and contamination of drinking water sources is not expected.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Residential exposure to momfluorothrin is characterized as short-term in duration. Applicator exposure is predominantly by dermal and inhalation routes. Postapplication exposure for adults (16+) and youth (11 < 16 years) is predominantly by dermal and inhalation routes and for children (1 < 2 years) by dermal, inhalation and incidental oral routes.

Incidental (Non-Dietary) Oral Ingestion (Short- to Intermediate-Term):
For short- to intermediate-term non-dietary incidental exposure in children, the no observed adverse effect level (NOAEL) of 25 mg/kg bw/day based on the results from two co-critical studies (rat 90-day dietary, rat oral gavage developmental toxicity) was selected for risk assessment. In the 90-day rat study, the NOAEL was based on liver findings and decreased body weight at the lowest observed adverse effect level (LOAEL) of 76 mg/kg bw/day. In the rat developmental toxicity study, the NOAEL was based on clinical signs of neurotoxicity in the dams at the LOAEL of 75 mg/kg bw/day. The selection of these studies is considered appropriate as they address target organ effects in the most sensitive species (rat), and are of a relevant duration for this exposure scenario. The target Margin of Exposure (MOE) is 300, which includes the standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, and a 3-fold database uncertainty factor for concerns relating to potential sensitivity of the young. As discussed in the *Pest Control Products Act* Hazard Characterization section, residual uncertainty regarding susceptibility of the young has been captured under the database uncertainty factor. Consequently, the *Pest Control Products Act* factor was reduced to 1-fold.

The offspring NOAEL of 14.7 mg/kg bw/day in the rat reproduction study was also given consideration for this scenario. This NOAEL was based on reductions in body weight at PND 21 and decreased spleen weight at the LOAEL of 36 mg/kg bw/day. There were no effects in offspring (including body weight) at earlier time points in the study. For the reasons outlined in the *Pest Control Products Act* Hazard Characterization section, it was felt that the use of the offspring NOAEL was likely conservative and that the NOAEL of 25 mg/kg bw/day from the co-critical rat studies noted above would be protective since it is lower than the LOAEL for pup toxicity (36 mg/kg bw/day).

Short- to Intermediate-Term Dermal:
For short- to intermediate-term dermal risk assessments for all populations, the NOAEL of 1000 mg/kg bw/day (highest dose tested) from the 28-day dermal toxicity study in rats was selected. This study is representative of the route of exposure, and was considered relevant for both the short- and intermediate-term scenarios since there was no pronounced evidence of increased toxicity following increased duration of dosing in rats over the short to intermediate-term duration. The target MOE is 300, which includes the standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, and a 3-fold database uncertainty factor for concerns relating to potential sensitivity of the young. For residential scenarios, the *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section.

Selection of this endpoint provides protection for the delayed vaginal opening observed in the rat dietary reproduction study at 106 mg/kg bw/day (NOAEL for this effect was 36 mg/kg bw/day). In the reproduction study, increased maternal liver weights were recorded at the same dose level as the delayed vaginal opening in the pups. Since the liver was examined in the 28-day rat dermal study and no adverse effects were seen at the limit dose of 1000 mg/kg bw/day, use of this NOAEL is considered protective of the delayed vaginal opening endpoint.

Short- to Intermediate-Term Inhalation:
For short- to intermediate-term inhalation risk assessments for all populations, the no observed adverse effect concentration (NOAEC) of 0.150 mg/L (26 mg/kg bw/day) from the 28-day inhalation toxicity study in rats was selected. This study represents the relevant route of exposure for this scenario. The lowest observed adverse effect concentration (LOAEC) of 0.300 mg/L (52 mg/kg bw/day) was based on increased liver weight, alterations in clinical chemistry parameters and clinical signs of neurotoxicity (tremors). The target MOE is 300, which includes the standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, and a 3-fold database uncertainty factor for concerns relating to potential sensitivity of the young. For residential scenarios, the *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section.

Selection of this endpoint was considered appropriate for assessment of both short-term and intermediate-term scenarios as there was no pronounced evidence of increased toxicity following increased duration of dosing over the short to intermediate-term duration.

Short- to Intermediate-Term Aggregate Assessment:
For aggregate risk assessment for the general population (including pregnant women, infants and children) for short-to intermediate-term duration, the selected toxicological endpoints are liver findings and clinical signs of neurotoxicity. For oral exposure, the NOAEL of 25 mg/kg bw/day from two co-critical studies (90-day dietary study in rats and oral gavage developmental toxicity study in rats) was selected. Liver findings and clinical signs of neurotoxicity (tremors) were observed in the 90-day and developmental toxicity studies, at the LOAELs of 76/75 mg/kg bw/day, respectively. For the inhalation aggregate risk assessment, it was considered appropriate to use the NOAEC of 0.150 mg/L (26 mg/kg bw/day) from the 28-day inhalation study in rats. Increased liver weight and clinical signs of neurotoxicity (tremors) were observed at the next highest concentration of 0.300 mg/L (52 mg/kg bw/day). It was not considered necessary to include the dermal route in the aggregate risk assessment as liver effects and clinical signs of neurotoxicity were not evident following dermal dosing in rats.

Selection of these endpoints was considered appropriate for assessment of both short-term and intermediate-term scenarios as there was no pronounced evidence of increased toxicity following increased duration of dosing over the short to intermediate-term duration.

For both the oral and inhalation routes of exposure, a target MOE of 300 was selected. This target MOE includes a 10-fold uncertainty factor for interspecies extrapolation, a 10-fold uncertainty factor for intraspecies variability and a 3-fold database uncertainty factor for concerns related to potential sensitivity of the young. The *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section.

Cancer Assessment

As previously discussed, an increased incidence of liver tumours was observed in rats following chronic dosing. An MOA for tumour induction was proposed similar to that of phenobarbital. The proposed MOA was deemed plausible, despite some limitations, and the overall weight of evidence was sufficient to conclude that a linear low dose extrapolation (q_1*) approach to the cancer risk assessment may be overly conservative. For these reasons, a threshold approach for liver tumours was applied for the cancer risk assessment.

For oral and inhalation risk assessments, the selected NOAEL (25 mg/kg bw/day) also represents the NOAEL for pre-neoplastic liver lesions in rats, and therefore it was considered protective of the observed liver tumours. Since there were no liver effects observed up to the limit dose in the 28-day dermal study, selection of this NOAEL is considered protective of the preneoplastic liver changes observed following long-term dosing in rats.

3.4.1.1 Dermal Absorption

A dermal absorption value was not established as a route-specific study was chosen for the dermal NOAEL.

3.4.2 Residential Exposure and Risk Assessment

3.4.2.1 Handler Exposure and Risk

Residential applicator exposure is calculated based on the algorithm and default parameter values from the United States Environmental Protection Agency (USEPA) 2012 Residential SOP, Section 7 Indoor Environments. Indoor exposure is considered to adequately estimate exposure from outdoor use.

Using the default values in combination with toxicological endpoints, residential exposure is not expected to result in unacceptable risk when momfluorothrin is used according to label directions as the calculated MOEs exceeded the target MOE 300 (Appendix 1, Table 5).

3.4.2.2 Postapplication Exposure and Risk

Dermal and inhalation exposure for a short-term duration was calculated for adults (> 16) and youth (11 < 16 years). Inhalation, dermal and incidental-oral exposures for a short-term duration were calculated for children (1 < 2 years). A single postapplication risk assessment is presented for the products as their use patterns are similar.

All parameter values were derived from the 2012 USEPA Residential SOP for Indoor Environments for spot application (coarse spray) except for the application rate. The highest application rate of 6.15 $\mu g/cm^2$ was used to conduct the risk assessment. The proposed end-use products do not come with an applicator wand or nozzle so the product spray more closely resembles a coarse spray which corresponds to a deposited residue of 50% of the application rate. The proposed use of one end-use product on furniture is covered by the risk assessment for soft surfaces.

The calculated MOEs for spot (coarse spray) treatment on hard and soft surfaces generated MOEs above the target MOE of 300 (Appendix 1, Tables 6 to 9).

3.4.2.3 Combined Exposure

Based on toxicological information, the dermal and inhalation routes cannot be combined because there are no common effects; however, the individual routes can be combined for the applicator and post-application scenarios. When the two dermal exposures are combined and the two inhalation exposures are combined, all target MOEs are exceeded (Appendix 1, Table 10).

Based on common liver effects and tremors in the studies from which the inhalation and incidental oral endpoints were derived, these two routes of exposure were combined for children (1 < 2 years) (Appendix 1, Table 11). It is not recommended in the USEPA Residential SOP for Indoor Environments to combine object-to-mouth exposure with hand-to-mouth as it is considered overly conservative for total combined exposure.

3.4.2.4 Bystander Exposure and Risk

For bystanders, exposure is expected to be less than that of applicators and is considered to not be of concern.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

The physical and chemical characteristics of momfluorothrin are summarized in Appendix 1, Table 12. Transformation products, maximum formation in the environment and chemical structures, are discussed in Appendix I, Table 13. The environmental fate data for momfluorothrin are summarized in Appendix 1, Table 14.

Momfluorothrin is sparingly soluble in water, has low volatility, and does not have a dissociable moiety (Table 12). The log K_{ow} of 2.95 is close to the cut-off value indicating a potential for bioaccumulation. A bioconcentration study in fish showed, however, that under more environmentally relevant conditions, momfluorothrin is not likely to bioaccumulate. Residues of momfluorothrin were not detected in fish tissue after the first day of exposure. Bioconcentration factor (BCF) values of 600-612 were determined from total [^{14}C]-residues, which was attributed to the presence of transformation products.

Momfluorothrin is stable to hydrolysis at pH 4 and pH 7, but undergoes hydrolysis at pH 9, with half-lives of approximately 12 days at 20°C and 7 days at 25°C. A study of photolysis in water (pH 4) indicated a half-life of approximately 13 days under continuous illumination, equivalent to approximately 31.7 US solar days at 40°N latitude (based on 10.2 hours sunlight/day). Based on this half-life, phototransformation of momfluorothrin in water will not be a significant route of transformation in the environment. Momfluorothrin undergoes rapid microbial degradation under aerobic conditions in soil, with half-lives less than five days, and in water-sediment systems, with half-lives of less than three days. The soil organic carbon-water partitioning coefficient (K_{oc} ranging from 1033 to 4344) for different soils and sediments suggest a low mobility of momfluorothrin in the environment.

Eight isomers are associated with momfluorothrin. The major isomer (RTZ) is present in the technical grade active ingredient at >80%. Studies of fate and biotransformation showed that, although isomerization occurs in the presence of light, it should not be a significant factor in the fate of momfluorothrin in the environment. When isomerization did occur, all other isomers were detected at < 5% of applied radioactivity (AR). Isomerization did not take place in the dark.

A number of major transformation products were detected in the fate studies and are summarized in Appendix 1, Table 13. MFOA and CMCA are products of hydrolytic cleavage and were the only major transformation products in hydrolysis and photolysis studies. The other transformation products were detected in biotransformation studies in soil and water/sediment. For further information on their formation and chemical structures, see Appendix 1, Table 13. Due to the limited potential for exposure to the environment, from crack and crevice and spot treatments with an aerosol can, no further information are requested at this time regarding the environmental fate and ecotoxicology of the transformation products.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. Where EECs cannot be practically determined, a more qualitative risk assessment approach may be taken.

A quantitative risk characterization was not conducted for momfluorothrin because limited environmental exposure is expected from the use of this product as a household aerosol spray. Products containing momfluorothrin are proposed to be used as a crack and crevice or spot treatment indoors and outdoors to control flying and crawling insects. Insects are controlled by direct contact with the insecticide sprayed from an aerosol can. These products may be used to control insects on the outside surfaces of buildings, in cracks and crevices, as well as via spot treatment at picnic areas. The contents of wasp, hornet, yellowjacket, or ant nests are not to be treated with these products. Thus, only small, limited areas/infestations are being treated where insect pests are visible, thereby limiting the exposure and risk to non-target organisms in the environment.

End-use products of momfluorothrin are formulated with either piperonyl butoxide (a synergist used to enhance the toxicity of certain pesticide active ingredients) or d-phenothrin (a synthetic pyrethroid insecticide). Due to the nature of the use, the limited potential for exposure of non-target terrestrial and aquatic organisms in the environment, any additional risks related to these co-formulations is expected to also be very limited.

Environmental toxicology data for various terrestrial and aquatic organisms were submitted and reviewed, and are summarized in Appendix 1, Table 15. Momfluorothrin is practically non-toxic to most terrestrial organisms that were studied but highly toxic through the contact route to honeybees. Momfluorothrin is also very highly toxic to aquatic organisms (in other words, fish and *Daphnia magna*). Based on this information, hazard-based label statements will, therefore, be required to inform users of the toxicity of momfluorothrin to these organisms.

5.0 Value

5.1 Effectiveness Against Pests

Momfluorothrin Flying and Crawling Insect Killer Spray:
Nine laboratory trials supported a claim that Momfluorothrin Flying and Crawling Insect Killer Spray kills ants, cockroaches, house flies, hornets, mosquitoes, paper wasps, spiders, stable flies and yellow jackets on contact.

MGK 29831:
Four laboratory trials supported a claim that MGK 29831 kills fruit flies, house flies, horn flies, stable flies, Indian meal moths and mosquitoes on contact. Extrapolations from these data supported a claim that MGK 29831 kills lesser house flies, Mediterranean flour moths, Angoumois grain moths and clothes moths on contact.

MGK 29871 and MGK 29872:
Four laboratory trials supported a claim that MGK 29871 and MGK 29872 kill wasps, hornets and yellow jackets on contact.

5.2 Non-Safety Adverse Effects

The following cautionary statement is present on all labels: "Users should test a small, inconspicuous area first to ensure there are no adverse effects such as staining, discolouration or corrosion prior to treating an entire area."

In addition, the following statement appears on the labels of MGK 29871 and MGK 29872: "This product may stain or adversely affect vinyl, painted, and plastic surfaces. Avoid application to asphalt roofing shingles as staining may occur. Test in an inconspicuous area and re-check in a few hours before using in areas where spray may contact these surfaces."

5.3 Consideration of Benefits

5.3.1 Survey of Alternatives

The majority of domestic class insecticides registered against the same insect and spider pests found indoors and outdoors are pyrethroids. Ten of these are under re-evaluation (REV2011-05). Borates are also registered but certain products have been proposed for phase out (PRVD2012-03). Older conventional chemistries registered against some of these pests are propoxur, dichlorvos, paradichlorobenzene and naphthalene. Some uses of propoxur are being phased out (biting fly control, indoor uses of domestic class products except bait trays; REV2014-01). Abamectin, chlorpyrifos and thiamethoxam are insecticides in registered ant and/or cockroach baits. German cockroach extract and (Z)-9-tricosene are registered to trap and kill German cockroaches and house flies, respectively. Non-conventional insecticides against some of the labelled pests include diatomaceous earth/silicon dioxide, d-limonene and soybean oil.

5.3.2 Compatibility with Current Management Practices Including Integrated Pest Management

All products can be used against labelled pests with other pest control practices such as sanitation and structural repairs.

5.3.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

The potential for the development of resistance in pests is expected to be similar to that of other pyrethroids. Resistance has been reported for some of the labelled pests.

5.4 Supported Uses

Momfluorothrin Flying and Crawling Insect Killer Spray kills ants, cockroaches, house flies, hornets, mosquitoes, paper wasps, spiders, stable flies and yellow jackets on contact.

MGK 29831 kills Angoumois grain moths, clothes moths, fruit flies, house flies, horn flies, Indian meal moths, lesser house flies, Mediterranean flour moths, mosquitoes and stable flies on contact.

MGK 29871 and MGK 29872 kill wasps, hornets and yellow jackets on contact.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy: in other words, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, momfluorothrin was assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

> Momfluorothrin does not meet all Track 1 criteria, and is not considered a Track 1 substance. See Appendix I, Table 16, for comparison with Track 1 criteria.

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5 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[6]. The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[8], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

Technical grade momfluorothrin and the associated products Sumifreeze Manufacturing Use Product, Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 2983, MGK 2987, MGK 29831, MGK 29871 and MGK 29872 do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for momfluorothrin is adequate to define the majority of toxic effects that may result from exposure. In short-term and chronic studies on laboratory animals, the primary targets of toxicity were the neurological system and the liver. Momfluorothrin was not considered to be genotoxic. Liver tumours were observed in the rat, but not the mouse following chronic exposure. Despite limitations in the proposed MOA for the liver tumours, the overall weight of evidence allowed for a threshold approach for the cancer risk assessment. Momfluorothrin was not teratogenic in rats or rabbits, and did not cause any adverse effects on reproduction in rats. There was a low level of concern for increased sensitivity of the offspring; however, residual uncertainty remains regarding susceptibility of the young to the effects of pyrethroids. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

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6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643; *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613, *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

8 DIR2006-02, *PMRA Formulants Policy.*

Residential exposure to individuals handling momfluorothrin, or residing in treated indoor and outdoor areas, is not expected to result in unacceptable risk when momfluorothrin is used according to label directions.

7.2 Environmental Risk

Momfluorothrin has low water solubility, low vapour pressure, and is not expected to bioaccumulate in aquatic organisms. Momfluorothrin is non-persistent in the environment as it undergoes rapid microbial transformation under aerobic conditions in soil and water/sediment systems. Momfluorothrin will bind to soil and sediment, and is not expected to be mobile in soil.

Momfluorothrin is practically non-toxic to most terrestrial organisms that were studied but highly toxic to honeybees through the contact route. Momfluorothrin is also very highly toxic to aquatic organisms (for example, fish and *Daphnia magna*).

All of the end-use products are aerosol cans for domestic use as crack and crevice or spot treatments against crawling and flying insects. As such, due to the limited nature of these uses, the potential for exposure of non-target terrestrial and aquatic organisms in the environment is expected to be very limited. The risk to non-target organisms in the environment is not expected to be a concern if the formulated products are used according to the proposed use directions. Hazard label statements are, however, required to inform users of the toxicity of momfluorothrin to these organisms.

7.3 Value

Momfluorothrin is a new pyrethroid insecticide that rapidly immobilizes insect and spiders pests after treatment. This may reduce the distance the target pest travels after treatment and allow easier disposal of dead insects and spiders. The combination of momfluorothrin with d-phenothrin found in Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 29871 and MGK 29872 may improve the efficacy against pests compared to either active ingredient alone. MGK 29831 combines momfluorothrin with a synergist, piperonyl butoxide, which increases the efficacy against house flies compared to momfluorothrin alone.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Momfluorothrin Technical Grade, as well as three manufacturing concentrates: Sumifreeze Manufacturing Use Product, MGK 2983 and MGK 2987; and four domestic class end-use products: Momfluorothrin Flying and Crawling Insect Killer Spray, MGK 29831, MGK 29871 and MGK 29872 used to control a variety of insect and spiders species found indoors and outdoors at residential locations.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

♀	female
♂	male
µg	micrograms
a.i.	active ingredient
ADI	acceptable daily intake
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase
ATPD	area treated per day
BCF	bioconcentration factor
BrdU	bromodeoxyuridine
bw	body weight
bwg	bodyweight gain
CAR	constitutive androstane receptor
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
cm^2	centimetre(s) squared
cm^3	centimetre(s) cubed
d	day(s)
DACO	data code
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
ε	molar extinction coefficient ($L\ mol^{-1}\ cm^{-1}$)
EC_{50}	effective concentration on 50% of the population
EEC	estimated environmental concentration
ET	exposure time
FL-HDPE	Fluorinated high-density polyethylene
FOB	functional observational battery
F1	first generation
F2	second generation
fc	food consumption
g	gram(s)
GC-MS/MS	Gas chromatography coupled to Tandem Mass Spectrometry
GD	gestation day
GGT	gamma-glutamyl transferase
h	hour(s)
HDPE	High-density polyethylene
HDT	highest dose tested
IC_{50}	inhibitory concentration on 50% of the population
ID	identification
IUPAC	International Union of Pure and Applied Chemistry
K_{ads}	soil adsorption coefficient
K_{des}	soil desorption coefficient

kg	kilogram(s)
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
m^2	meter(s) squared
m^3	meter(s) cubed
mg	milligram(s)
mL	millilitre(s)
M_{label}	mass of active ingredient applied
MAS	maximum average score
MIS	maximum irritation score
MOA	mode of action
MOE	margin of exposure
mol	mole(s)
N/A	not applicable
nm	nanometre(s)
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NZW	New Zealand white
P	parental generation
Pa	Pascal
PHED	Pesticide Handlers Exposure Database
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	postnatal day
ppm	parts per million
PROD	pentoxyresorufin *o*-dealkylase
q_1^*	cancer potency factor
rel	relative
RT_{25}	residual time to 25% mortality
SER	smooth endoplasmic reticulum
SOP	standard operating procedure
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TC	transfer coefficient
TSH	thyroid stimulating hormone
TSMP	Toxic Substances Management Policy
UDP-GT	uridine diphosphate glucuronyltransferase

US	United States
USEPA	United States Environmental Protection Agency
UV	ultraviolet
wt	weight(s)

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Soil	Not stated	S-1563 RTZ S-1563 RTE	GC/MS/MS	0.01 mg/kg in soil	PMRA # 2266973

Table 2a Toxicity Profile of Sumifreeze Manufacturing Use Product (15.7% a.i.)

Study Type/Animal/PMRA #	Study Results
Acute Oral LD_{50} Toxic Class (423) Rat PMRA #2266651	LD_{50} ♀ > 2000 mg/kg bw Low toxicity
Acute Dermal LD_{50} Rat PMRA #2266653	LD_{50} ♂♀ > 2000 mg/kg bw Low toxicity
Acute Inhalation LC_{50} Rat PMRA #2266655	LC_{50} > 1030 mg/m^3 Slight toxicity
Primary Eye Irritation Rabbit PMRA #2266659	MAS (24, 48, 72 hours) =14.8 /110 MIS = 23/110 at 24 hours All scores not 0 by 72 hours Mildly irritating
Primary Skin Irritation Rabbit PMRA #2266661	MAS (24, 48, 72 hours) = 0/8 MIS= 0/8
Skin Sensitization Buehler Guinea pig PMRA #2266663	Negative

Table 2b Toxicity Profile of Momfluorothrin Flying and Crawling Insect Killer Spray (0.1% momfluorothrin, 0.2% d-phenothrin)

Study Type/Animal/PMRA #	Study Results
Acute Oral LD_{50} Toxic Class (423) Rat PMRA #2266780	LD_{50} ♀ > 2000 mg/kg bw Low toxicity

Study Type/Animal/PMRA #	Study Results
Acute Dermal LD_{50} Rat PMRA #2266782	LD_{50} ♂♀ >2000 mg/kg bw Low toxicity
Acute Inhalation LC_{50} Rat PMRA #2266784	LC_{50} ♂♀ >0.523 mg/L Slight toxicity
Primary Eye Irritation Rabbit PMRA #2266788	MAS (24, 48, 72 hours) = 0/110 MIS = 1.3/110 at 1 hour Non irritating
Primary Skin Irritation Rabbit PMRA #2266790	MAS(24, 48, 72 hours) = 0.23/8 MIS= 0.7/8 at 1 and 24 hours Minimally irritating
Skin Sensitization Buehler Guinea pig PMRA #2266792	Negative

Table 2c Toxicity Profile of MGK 2983 (2.225% momfluorothrin, 17.8% piperonyl butoxide)

Study Type/Animal/PMRA #	Study Results
Acute Oral LD_{50} Up and Down (425) Rat PMRA #2267100	LD_{50} ♂♀ =550 mg/kg bw Moderately toxic
Acute Dermal LD_{50} Rat PMRA #2267102	LD_{50} ♂♀ >5000 mg/kg bw Low toxicity
Acute Inhalation LC_{50} Rat PMRA #2267103	LC_{50} ♂♀ >2.04 mg/L Low toxicity
Primary Eye Irritation Rabbit PMRA #2267105	MAS (24, 48, 72 hours) = 0/110 MIS = 9.3/110 Non-irritating
Primary Skin Irritation Rabbit PMRA #2267106	MAS (24, 48, 72 hours) = 0/8 MIS= 1.7/8 at 1 hour Non-irritating
Skin Sensitization LLNA Mouse PMRA #2267107	Stimulation Index = 8.51 Potential skin sensitizer

Table 2d Toxicity Profile of MGK 29831 (0.05% momfluorothrin, 0.39% piperonyl butoxide)

Study Type/Animal/PMRA #	Study Results
Acute Oral LD_{50} Up and Down (425) Rat PMRA#2267469	LD_{50} ♀ >5000 mg/kg bw Low toxicity
Acute Dermal LD_{50} Rat PMRA# 2267470 (Performed with MGK 2983)	LD_{50} ♂♀ > 5000 mg/kg bw Low toxicity
Acute Inhalation LC_{50} Rat PMRA# 2267471 (Performed with MGK 2983)	LC_{50} ♂♀> 2.04 mg/L Low toxicity
Primary Eye Irritation Rabbit PMRA# 2267472	MAS (24, 48, 72 hours) =0.23 /110 MIS =0.7 /110 at 1 and 24 hours Minimally Irritating
Primary Skin Irritation Rabbit PMRA# 2267473	MAS (24, 48, 72 hours) = 0.53/8 MIS= 3.0/8, at 1 hour Minimally Irritating
Skin Sensitization LLNA Mouse PMRA# 2267475 (Performed with MGK 2983)	Stimulation Index = 8.51 Potential skin sensitizer

Table 2e Toxicity Profile of MGK 2987 (5% momfluorothrin, 20% d-phenothrin)

Study Type/Animal/PMRA #	Study Results
Acute Oral LD_{50} Up and Down (425) Rat PMRA #2267153	LD_{50} ♀ = 985 mg/kg Moderately toxic
Acute Dermal LD_{50} Rat PMRA #2267154	LD_{50} ♂♀ > 5000 mg/kg bw

Study Type/Animal/PMRA #	Study Results
Acute Inhalation LC_{50} Rat PMRA #2267155	LC_{50} ♂ > 2.07 mg/L LC_{50} ♀ > 0.51 mg/L<2.07 mg/L Slightly toxic
Primary Eye Irritation Rabbit PMRA #2267157	MAS (24, 48, 72 hours) = 21.7/110 MIS = 27.3/110 Mildly irritating
Primary Skin Irritation Rabbit PMRA #2267159	MAS (24, 48, 72 hours) = 2/8 MIS= 2.6/8 at 24 hours Mildly irritating
Skin Sensitization LLNA Mouse PMRA #2267161	Stimulation Index = 2.81 Negative

Table 2f Toxicity Profile of MGK 29871 (0.05% momfluorothrin, 0.20% d-phenothrin)

Study Type/Animal/PMRA #	Study Results
Acute Oral LD_{50} Up and Down (425) Rat Performed with MGK 29872 PMRA #2267697	LD_{50} ♀ > 5000 mg/kg bw Low toxicity
Acute Dermal LD_{50} Rat Performed with MGK 2987 PMRA #2267698	LD_{50} ♂♀ > 5000 mg/kg bw Low toxicity
Acute Inhalation LC_{50} Rat Performed with MGK 29872 PMRA #2267699	LC_{50} ♂♀ >2.12 mg/L Low toxicity
Primary Eye Irritation Rabbit PMRA #2267700	MAS (24, 48, 72 hours) = 0/110 MIS = 0/110 Non-irritating
Primary Skin Irritation Rabbit PMRA #2267701	MAS (24, 48, 72 hours) =0 /8 MIS= 0/8 Non-irritating

Study Type/Animal/PMRA #	Study Results
Skin Sensitization LLNA Mouse Performed with MGK 2987 PMRA #2267702	Stimulation Index = 2.81 Negative

Table 2g Toxicity Profile of MGK 29872 (0.05% momfluorothrin, 0.20% d-phenothrin)

Study Type/Animal/PMRA #	Study Results
Acute Oral LD_{50} Up and Down (425) PMRA #2267587	LD_{50} ♀ >5000 mg/kg bw Low toxicity
Acute Dermal LD_{50} Rat Performed with MGK 2987 PMRA# 2267589	LD_{50} ♂♀ > 5000 mg/kg bw Low toxicity
Acute Inhalation LC_{50} Rat PMRA#2267590	LC_{50}♂♀ >2.12 mg/L Low toxicity
Primary Eye Irritation PMRA #2267592	MAS (24, 48, 72 hours) =0.23 /110 MIS = 6.7/110 at 1 hour Minimally irritating
Primary Skin Irritation PMRA #2267596	MAS (24, 48, 72 hours) = 0.1/8 MIS=0.7 /8 at 1 hour Minimally irritating
Skin Sensitization LLNA Mouse Performed with MGK 2987 PMRA #2267702	Stimulation Index = 2.81 Negative

Table 3 Toxicity Profile of Technical Momfluorothrin

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted). Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study Type/Animal/PMRA #	Study Results
Metabolism and pharmacokinetics (single administration, Z and E isomers) Wistar rat PMRA #2299082	Momfluorothrin (S-1563) undergoes rapid absorption (90% for isomer Z, and 80% for isomer E). Excretion also occurs rapidly, nearing completion within two days and being fully complete by day 7. The major route of excretion for the Z isomer was feces in males (54% or 65% following low or high dose respectively), and urine in females (66% and 48% following low or high dose respectively). The urine was the major route for the E isomer in both sexes (67%/81% in males/females at the low dose; 64%/79% in males/females at the high dose). Excretion tended to be slightly slower in males. Excretion via expired air was negligible in both sexes and for both isomers. Administration of the Z-isomer to bile duct-cannulated rats at the low dose showed that approximately 52% of the administered radioactivity was excreted into the bile of both sexes by 3 days post-dose. For the E-isomer, biliary excretion represented 60% and 47% of the administered radioactivity in males and females, respectively. This indicates that the absorption rate was about 90% for the Z-isomer and over 80% for the E isomer. Distribution in organs and tissues was similar following single low or high dose of either isomer and was highest in liver, kidney and gastrointestinal tract and its contents. For both isomers, following either a single low or high dose, C^{14} residue in the whole body was approximately 0.2% of the administered dose in both sexes at 168 hours after administration. The major metabolic reactions of S-1563RTZ were: formation of Z-CMCA through cleavage of the ester linkage; oxidation of the methyl group in the propenyl group; demethylation of the methoxymethyl group; conjugation with glucuronic acid; oxidation of the methyl group in the cyclopropyl group; addition of sulfonic acid to the propenyl group; reduction of double bond in the propenyl group; oxidation of double bond in the propenyl group and isomerization of glucuronide The major metabolic reactions of S-1563RTE were: formation of E-CMCA through cleavage of the ester linkage; demethylation of the methoxymethyl group; conjugation with glucuronic acid; oxidation of the methyl group in the cyclopropyl group; oxidation of the methyl group in the propenyl group and isomerization of glucuronide.
Metabolism and pharmacokinetics (repeat administration) Wistar rat PMRA #2299081	Radioactivity was excreted almost entirely in urine and feces within the first 24 hours after the third dose. Residual radioactivity in the carcass was less than 0.1% at the end of the study. Tissue concentrations remained relatively constant at 6 hours following dosing at 10, 16, or 21 doses. Concentration is plasma was no longer detectable at 168 hours after the last dose. Accumulation of radioactivity to tissues was considered low. Excretion in urine and feces was not altered by repeated administration. Distribution of radioactivity and the composition of metabolites in tissues showed almost the same pattern during repeated administration.
Acute oral toxicity Sprague Dawley rat PMRA # 2299086	LD_{50} >2000 mg/kg bw (♂) Low Toxicity LD_{50} between 300-2000 mg/kg bw (♀) High toxicity

Study Type/Animal/PMRA #	Study Results
Acute dermal toxicity Sprague Dawley rat PMRA #2299091	LD_{50} > 2000 mg/kg bw Low toxicity
Acute inhalation toxicity Sprague Dawley rat PMRA # 2299093	LC_{50} >2030 mg/m^3 Low toxicity
Eye irritation NZW rabbit PMRA #2299089	Unwashed: MIS = 10.0 at 1 hour MAS (24, 48, 72 hours) = 1.6 Washed: MIS = 4.0 at 1 hour MAS (24, 48, 72 hours) = 0.23 Minimally irritating
Dermal irritation NZW rabbit PMRA #2299090	MIS = 0 MAS (24, 48, 72 hours) = 0 Non-irritating
Skin sensitization (Maximization method) Guinea pigs PMRA #2324610	Negative
90-Day oral toxicity (diet) Wistar rat PMRA #2324611	NOAEL = 23/25 mg/kg bw/day (300 ppm) LOAEL = 76/82 mg/kg bw/day; based on ↑brownish pigment in liver, ↑cholesterol, ↑phospholipids; ↑protein, ↑α-2-globulin (♂); ↓bw, ↓bwg (♀) **Recovery period:** bw of high dose animals was still below that of controls at the end of the recovery period; however, bwg was higher than that in controls, indicating the animals were recovering from this effect.
90-Day oral toxicity (capsule) Beagle dog PMRA #2299062	NOAEL = 200 mg/kg bw/day LOAEL = 600 mg/kg bw/day; based on clinical signs of toxicity (↑incidences of watery, mucus or discoloured feces and vomiting of mucus or feed), ↑liver wt, ↑cholesterol and triglycerides, liver histopathology (hepatocellular hypertrophy). There were no treatment-related findings by the end of the recovery period.
28-Day dermal toxicity Sprague Dawley rat PMRA #2266863	NOAEL = 1,000 mg/kg bw/day (HDT) A detailed clinical examination was performed (home cage, hand-held and open field).
28-day inhalation toxicity Sprague Dawley rat PMRA #2299094	NOAEC = 150 mg/m^3 (~26 mg/kg bw/day) LOAEC =300 mg/m^3 (~52 mg/kg bw/day); based on ↑liver wt, ↑cholesterol; clinical signs (tremors, rigidity), ↑AST (♂); ↑phospholipids (♀)

Study Type/Animal/PMRA #	Study Results
52- week Chronic toxicity (diet) Wistar rat PMRA #2299063	NOAEL (♂) = 27.4 mg/kg bw/day LOAEL (♂) = 82.6 mg/kg bw/day; based on ↑cholesterol; ↑α2-globulin, ↑GGT, ↑phospholipids, enlarged liver, ↑rel liver wt, ↑brown pigment in liver and kidneys, ↑hepatocellular hypertrophy NOAEL (♀) = 12.4 mg/kg bw/day LOAEL (♀) = 33.5 mg/kg bw/day; based on ↓bw, ↓ bwg, ↑phospholipids, ↑rel liver wt, ↑hepatocellular hypertrophy, ↑brown pigment in liver No effects on FOB parameters were observed
78- week Oncogenicity (diet) CD-1 mice PMRA #2266865	NOAEL = 72/99 mg/kg bw/day LOAEL = 308/427 mg/kg bw/day; based on ↑liver wt, ↑hepatocellular hypertrophy; ↓bw , ↓ bwg (♂) **No evidence of carcinogenicity**
104-week Carcinogenicity (diet) Wistar rat PMRA #2266856	NOAEL = 23/28 mg/kg bw/day LOAEL = 73/88 mg/kg bw/day; based on ↓bw, ↓bwg, ↑hepatocellular hypertrophy, ↑brownish pigment in the liver; ↑rel liver wt, ↑cystic degeneration of the liver (♂), ↑incidence of hepatocellular adenomas, carcinomas, adenomas and carcinomas combined (♂) **Evidence of carcinogenicity**
Developmental toxicity (gavage) Sprague Dawley rat PMRA #2299092	**Maternal Toxicity** NOAEL = 25 mg/kg bw/day LOAEL = 75 mg/kg/day; based on tremors observed 2-3 hours after administration (GD 15-19) **Developmental Toxicity** NOAEL = 75 mg/kg bw/day (HDT) LOAEL not established **No evidence of sensitivity of the young or malformations**
Developmental toxicity (gavage) New Zealand White rabbits PMRA #2299070	**Maternal Toxicity:** NOAEL = 1000 mg/kg bw/day (HDT) LOAEL not established **Developmental Toxicity:** NOAEL = 1000 mg/kg bw/day (HDT) LOAEL not established **No evidence of sensitivity of the young or malformations**

Study Type/Animal/PMRA #	Study Results
2-Generation reproduction Wistar rat (diet) PMRA #2266864	**Parental Toxicity:** NOAEL (♂) = 32.1 mg/kg bw/day (500 ppm) LOAEL (♂) = 95.2 mg/kg bw/day (1500 ppm); based on ↓bw (F1), ↑liver wt (F1), ↓fc (P&F1), enlarged liver, ↑hepatocellular hypertrophy; ↓bw (P♂), ↓bwg (P♂); ↑liver wt (P♀) NOAEL (♀) = 106.3 mg/kg bw/day (1500 ppm) (HDT) LOAEL (♀) not established **Offspring Toxicity:** NOAEL = 14.7 mg/kg bw/day (200 ppm) LOAEL = 35.5 mg/kg bw/day (500 ppm); based on ↓bw PND21 (F1/F2),↓spleen wt (F1♂ & F1/F2♀) **Reproductive Toxicity:** NOAEL = 95.2/106.3 mg/kg bw/day (1500 ppm) (HDT) LOAEL not established **Evidence of sensitivity of the young**
Bacterial reverse mutation S. typhimurium TA98, TA100, TA1535, TA1537; E. coli WP2 uvrA PMRA #2299078	Negative
In vitro mammalian cell gene mutation Chinese Hamster V79 Cells PMRA #2266875	Negative
In vitro mammalian chromosome aberration Chinese Hamster Lung Cells PMRA #2299084	Positive (with metabolic activation) No increases in the incidence of structurally or numerically aberrant cells were observed in the absence of metabolic activation. In both experiment 1 and 2, a marginal increase of structurally aberrant cells (mostly chromatid breaks and exchanges) was reported with metabolic activation. Marginal positive result = incidence of structurally aberrant cells (excluding gaps) of ≥5% and <10%
Rat bone marrow micronucleus assay (gavage) Sprague Dawley rats PMRA #2299085	Negative In males, tremors were observed at ≥300 mg/kg bw and soft stools were observed at ≥150 mg/kg bw. In females, deaths (2/20 animals) and tremors were noted at 200 mg/kg bw.

Study Type/Animal/PMRA #	Study Results
Unscheduled DNA synthesis in mammalian cultured cells PMRA #2299088	Negative
Acute neurotoxicity (gavage) Sprague Dawley rat PMRA #2299073	NOAEL = 80 mg/kg bw LOAEL = 200 mg/kg bw; based on straub tail; ↑salivation (♂); mortality (1♀ on day following dosing), ↑tremors (♀)
Acute neurotoxicity (range-finding) (gavage) Sprague Dawley rat PMRA #2266866	NOAEL not established as study was considered supplemental Effects at 60 mg/kg bw included ↑miosis, ↑twitch, straub tail (♀). Tremors and ↑salivation in ♂ occurred at the next highest dose level.
13-Week neurotoxicity screening battery (diet) Wistar rat PMRA #2299072	NOAEL = 37/41 mg/kg bw/day LOAEL = 127/135 mg/kg bw/day; based on ↓bw; ↓bwg (♂) No evidence of neurotoxicity
28 Day immunotoxicity (diet) Wistar rat PMRA #2266862	NOAEL =81 mg/kg bw/day (1000 ppm) LOAEL = 241 mg/kg bw/day (3000 ppm); based on ↓bwg and fc (Day 0-3 only) No evidence of an immuno-suppressive effect.
Effects on ♂ mouse liver – time course analysis (diet) ICR mouse PMRA #2266855	<u>7 days</u> **740 mg/kg bw/day (5500 ppm)**: ↑ liver wt, centrilobular hepatocellular hypertrophy , ↑ BrdU labelling, ↑ CYP2B10 mRNA expression level. <u>14 days</u> **760 mg/kg bw/day (5500 ppm):** ↑ liver wt, centrilobular hepatocellular hypertrophy, ↑ BrdU labelling, ↑ CYP2B10 mRNA expression level. CYP4A10 enzymes induced only slightly after 7 and 14 days of dosing. Overall, the data indicate that the alterations induced by momfluorothrin in the ♂ mouse may be associated with mitogenesis via CAR activation.

Study Type/Animal/PMRA #	Study Results
Effects on ♂ mouse liver – dose response and reversibility (diet) ICR mouse PMRA #2266854	Main study **≥73 mg/kg bw/day (600 ppm):** ↑ PROD activity. **≥286 mg/kg bw/day (2500 ppm):** ↑ liver wt, ↑ BrdU labelling, centrilobular hepatocellular hypertrophy. **636 mg/kg bw/day (5500 ppm):** ↑ liver wt, ↑ lauric acid hydroxylation activity, proliferation of smooth endoplasmic reticulum (electron microscopy; not examined at lower doses). No evidence of peroxisome proliferation via electron microscopy. Recovery phase No treatment-related effects on the parameters examined at 681 mg/kg bw/day (5500 ppm). Overall, these findings demonstrate that the alterations induced by momfluorothrin in ♂ mice are reversible and suggest that momfluorothrin induces mitogenesis in the ♂ mouse liver via CAR activation.
Effects on ♀ mouse liver – time course analysis, dose response and reversibility (diet) ICR mouse PMRA #2266853	Main study – 7 days **≥69 mg/kg bw/day (600 ppm):** ↑ PROD activity, ↑ lauric acid hydroxylation activity. **≥292 mg/kg bw/day (2500 ppm):** ↑ liver wt, ↑ BrdU labelling, centrilobular hepatocellular hypertrophy. **492 mg/kg bw/day (5500 ppm):** proliferation of smooth endoplasmic reticulum (electron microscopy; not examined at lower doses). No evidence of peroxisome proliferation via electron microscopy. Main study – 14 days **549 mg/kg bw/day (5500 ppm):** ↑ liver wt, ↑ BrdU labelling, ↑ PROD activity, ↑ lauric acid hydroxylation activity, centrilobular hepatocellular hypertrophy. Recovery phase No treatment-related effects on the parameters examined at 674 mg/kg bw/day (5500 ppm). Overall, these findings demonstrate that the alterations induced by momfluorothrin in ♀ mice are reversible and suggest that momfluorothrin could induce mitogenesis in the ♀ mouse liver via CAR activation.

Study Type/Animal/PMRA #	Study Results
Effects on ♂ rat liver – time course analysis (diet) Wistar rat PMRA #2266852	7 days **147 mg/kg bw/day (3000 ppm):** ↑ rel. liver wt, centrilobular hepatocellular hypertrophy, ↑ CYP2B1/2 mRNA expression level, slight ↑ hepatocellular proliferation (BrdU labelling). 14 days **175 mg/kg bw/day (3000 ppm):** ↑ liver wt, centrilobular hepatocellular hypertrophy, ↑ CYP2B1/2 mRNA expression level, slight ↑ CYP3A1 mRNA expression level, slight ↑ hepatocellular proliferation (BrdU labelling). No induction of CYP1A2 or CYP4A1 after 7 or 14 days of dosing. Apart from the minimal hepatocellular proliferation, the data indicate that the alterations induced by momfluorothrin in ♂ rat liver may be associated with mitogenesis via CAR activation.
Effects on ♂ rat liver and thyroid – time course analysis at high dose (diet) Wistar rat PMRA #2266850	7 days **≥149 mg/kg bw/day (3000 ppm):** ↑ liver wt, centrilobular hepatocellular hypertrophy, ↑ BrdU labelling, ↑ hepatic UDP-GT. 14 days **≥160 mg/kg bw/day (3000 ppm):** ↑ liver wt, centrilobular hepatocellular hypertrophy, ↑ BrdU labelling, slight ↑ hepatic UDP-GT. **322 mg/kg bw/day (6000 ppm):**↑ rel. thyroid wt, thyroid follicular cell hypertrophy. No treatment-related effect on levels of thyroid hormones in serum. The slight ↑ in UDP-GT activity provides suggestive evidence of a weak effect on the hypothalamus-pituitary-thyroid axis, which may also be mediated by CAR activation.
Effects on ♂ rat liver – time course analysis, dose response and reversibility (diet) Wistar rat PMRA #2266851	Main study – 7 days **≥163 mg/kg bw/day (3000 ppm):** ↑ liver wt, ↑ PROD activity, slight ↑ lauric acid hydroxylation activity, centrilobular hepatocellular hypertrophy. Main study – 14 days **≥166 mg/kg bw/day (3000 ppm):** ↑ liver wt, enlarged liver, centrilobular hepatocellular hypertrophy. No evidence of proliferation of smooth endoplasmic reticulum or peroxisome proliferation via electron microscopy after 7 or 14 days of dosing. Recovery phase No treatment-related effects on the parameters examined at 168 mg/kg bw/day (3000 ppm). Apart from the lack of BrdU labelling data, the results indicate that momfluorothrin may induce liver tumour formation through mitogenesis mediated by CAR activation.

Study Type/Animal/PMRA #	Study Results
Effect on ♂ rat liver and thyroid – second study for dose response analysis (diet) Wistar rat PMRA #2266849	**≥76 mg/kg bw/day (1500 ppm):** ↑ rel. liver wt, ↑ BrdU labelling **137 mg/kg bw/day (3000 ppm):** ↑ liver wt, enlarged liver, diffuse hepatocellular hypertrophy, ↑ PROD activity. The study provides evidence of the key events in liver tumour induction associated with mitogenesis via CAR activation
Effect on ♀ rat liver – time course and dose response analysis (diet) Wista rat PMRA #2266848	7 days **≥80 mg/kg bw/day (1500 ppm):** ↑ rel. liver wt, ↑ BrdU labelling, slight ↑ PROD activity. **151 mg/kg bw/day (3000 ppm):** ↑ liver wt, diffuse hepatocellular hypertrophy. 14 days **164 mg/kg bw/day (3000 ppm):** ↑ rel. liver wt, ↑ BrdU labelling , ↑ PROD activity No treatment-related effect on lauric acid hydroxylation. The data indicate that the alterations induced by momfluorothrin in ♂ rat liver were replicated in ♀ rats and provide evidence that the liver tumours induced by momfluorothrin are likely associated with mitogenesis via CAR activation.
Effect on thyroid gland of ♂ rats (diet) Wistar rat PMRA #2266847	7 days **≥146 mg/kg bw/day (3000 ppm):** ↑ liver wt, diffuse hepatocellular hypertrophy, thyroid follicular cell hypertrophy, slight ↑ TSH, slight ↓ T4. **407 mg/kg bw/day (10,000 ppm):** enlarged liver. 14 days **≥157 mg/kg bw/day (3000 ppm):** ↑ liver wt, diffuse hepatocellular hypertrophy, thyroid follicular cell hypertrophy. **497 mg/kg bw/day (10,000 ppm):** enlarged liver, dark liver, slight ↑ TSH, slight ↓ T4. No treatment-related effect on T3 levels in serum. Overall, the data suggest that the alterations induced by momfluorothrin in ♂ rat liver are consistent with those seen in previous MOA studies and, therefore, add more support to the argument that the liver tumours induced by momfluorothrin are associated with mitogenesis via CAR activation. Data for disruption of the thyroid-hypothalamus-pituitary status are suggestive of an effect but very slight and principally seen at a dose in excess of the level causing liver tumours (10,000 ppm).

Study Type/Animal/PMRA #	Study Results
In vitro evaluation for role of CAR in the induction of CYP2B1/2 mRNA expression in cultured rat hepatocytes Primary rat hepatocytes PMRA #2266833	**Momfluorothrin :** ↑ CYP2B1/2 expression in normal hepatocytes; no effect on CYP2B1/2 expression in hepatocytes transfected with CAR-siRNA. **Z-CMCA**: ↑ CYP2B1/2 expression in normal hepatocytes, slight ↓ CYP2B1/2 expression in hepatocytes transfected with CAR-siRNA. Overall, the data suggest an operable CAR knock out gene in this in vitro test system and add further support to the argument that the rat liver tumours induced by momfluorothrin are likely associated with mitogenesis via CAR activation.

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Momfluorothrin

Exposure Scenario	Study	Point of Departure and Endpoint	Target MOE[1]
Incidental (non-dietary) oral (short-, intermediate term)	90-day dietary and developmental toxicity studies in rat (co-critical)	NOAEL = 25 mg/kg bw/day; based on liver findings and body weight effects (90-day study) and clinical signs of neurotoxicity (tremors) (developmental toxicity study)	300
Short-, intermediate-term dermal	28-day dermal toxicity study in rats	NOAEL = 1000 mg/kg bw/day (highest dose tested)	300
Short-, intermediate-term inhalation	28-day inhalation study in rats	NOAEC = 0.150 mg/L (26 mg/kg bw/day); based on increased liver weight and clinical signs of neurotoxicity (tremors)	
Aggregate risk assessment – based on liver findings and clinical signs of neurotoxicity			
Short-, intermediate term aggregate risk assessment	Oral: 90-day dietary and developmental toxicity studies in rat (co-critical) Inhalation: 28-day inhalation study in rats	Oral: NOAEL = 25 mg/kg bw/day; based on liver findings and body weight effects (90-day study) and clinical signs of neurotoxicity (tremors) (developmental toxicity study) Inhalation: NOAEC = 0.150 mg/L (26 mg/kg bw/day); based on increased liver weight and clinical signs of neurotoxicity (tremors)	300
	Dermal: not required (no effects noted)		
Cancer	Cancer risk (threshold) was addressed through the selected toxicology endpoints		

1 MOE refers to a target MOE for occupational and residential assessments

Table 5 Residential Applicator Exposure from Indoor and Outdoor Use

Unit Exposure (µg/kg a.i. handled)		ATPD (cans / day)	Application Rate (kg product/day) [2]	Dermal Exposure (mg/kg bw/day) [3]	Dermal MOE [4]	Inhalation Exposure (mg/kg bw/day) [3]	Inhalation MOE [4]
Dermal [1]	Inhalation						
816000	6610	0.5	0.100	0.00102	9.80×10^{3}	4.13×10^{-6}	6.29×10^{6}

[1] short sleeves, short pants and no gloves taken from the USEPA 2012 Residential SOP which used PHED aerosol data.
[2] Application Rate (kg product/day) = ATPD (cans/day) × Net Contents (g/can) × Conversion Factor (kg/1000 g)
[3] Exposure (mg/kg bw/day) = Application Rate (kg product/day) × Guarantee (%) × Unit Exposure (µg/kg a.i. handled) × Unit Conversion (mg/ 1000 µg) ÷ 80 kg bw
[4] MOE = NOAEL (mg/kg bw/day) ÷ Exposure, Target MOE = 300

Table 6 Indoor Inhalation Exposure from Momfluorothrin

Lifestage	Application Rate (kg a.i./L)	Amount Handled (L/day)	Mass of a.i. (mg; M_{label})	Exposure Time (hour)	Inhalation Exposure (mg/kg/day)	Inhalation MOE
Adults	9.66×10^{-4}	0.104	100	16	1.45×10^{-7}	1.79×10^{8}
Youths 11 < 16 years				15	1.86×10^{-7}	1.40×10^{8}
Children 1 to < 2 years				18	6.24×10^{-7}	4.17×10^{7}

Table 7 Child (1-2 year) Object-to-Mouth Exposure to Momfluorothrin

Exposure Scenario	Deposited Residue (µg/cm^2)	Fraction of residue transferred to object	Object Residue (µg/cm^2)	Exposure Time (hours/day)	Extraction by Saliva	Incidental Oral Exposure (mg/kg/day)	Incidental Oral MOE
Perimeter / Spot (Coarse)							
Soft Surfaces	3.08	0.06	0.185	4	0.48	0.00241	10400
Hard Surfaces		0.08	0.246	2	0.48	0.00161	15600

Table 8 Dermal Exposure to Momfluorothrin from Treated Hard and Soft Surfaces

Exposure Scenario		Lifestage	Deposited Residue (ug/cm^2)	Fraction transferred	Transferable Residue (ug/cm^2)	TC (cm^2/ hour)	ET (hour/ day)	Dermal Exposure (mg/kg/day)	Dermal MOE
Perimeter / Spot (Coarse)	Soft Surfaces	Adults	3.08	0.06	0.1845	6,800	8	0.1255	7970
		Youth 11 < 16 years			0.1845	5,600	5	0.09063	11000
		Children 1 < 2 years			0.1845	1,800	4	0.1208	8280
	Hard surfaces	Adults		0.08	0.246	6,800	2	0.04182	23900
		Youth 11 < 16 years			0.246	5,600	1	0.02417	41400
		Children 1 < 2 years			0.246	1,800	2	0.08051	12400

Table 9 Child (1-2 year) Hand-to-Mouth Exposure to Momfluorothrin

Exposure Scenario	Fraction a.i. on hands	Dermal Exposure (mg)	Surface area of 1 hand (cm^2)	Hand residue loading (mg/cm^2)	Fraction of hand mouthed	Exposure Time (hours/day)	Incidental Oral Exposure (mg/kg/day)	Incidental Oral MOE
Perimeter/Spot (Coarse)								
Soft Surfaces	0.15	1.33	150	0.000664	0.13	4	0.01812	1380
Hard Surfaces		0.886		0.000443		2	0.006041	4140

Table 10 Combined Applicator and Postapplicaton Re-entry Exposure for Adults

Applicator Dermal MOE	Postapplication Dermal MOE	Combined Dermal MOE [1]	Applicator Inhalation MOE	Postapplication Inhalation MOE	Combined Inhalation MOE [1]
9.80×10^5	7970	7900	6.29×10^6	1.79×10^8	6.08×10^6

[1] Combined MOE = 1/[(1/Applicator MOE) + (1/Postapplication MOE)]; Target MOE = 300

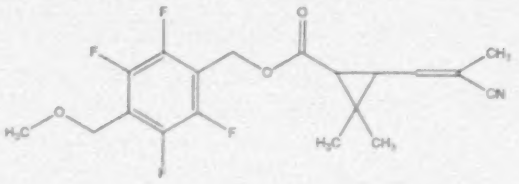
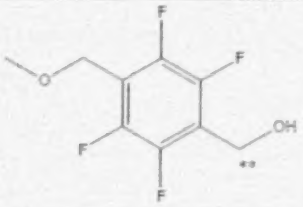
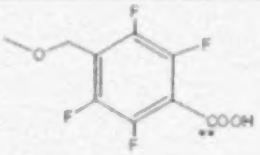
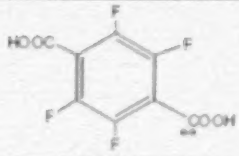
Table 11 Combined Inhalation and Oral Exposure for a Child (1-2 years)

Exposure Scenario	Incidental Oral Exposure (mg/kg/day)	Incidental Oral MOE	Inhalation Exposure (mg/kg bw/day)	Inhalation MOE	Combined MOE
Perimeter/Spot (Coarse)					
Soft Surfaces	0.01812	1380	6.24×10^{-7}	4.17×10^7	1380
Hard Surfaces	0.006041	4140			4140

Table 12 Physical and Chemical Properties of Momfluorothrin

Property	Value	Comments
Water solubility	0.933 mg/L	Sparingly soluble
Vapour pressure	2.5×10^{-7} Pa at 20°C	Low volatility
Henry's Law Constant	1.024×10^{-4} Pa m^3/mol	Not volatile from water surface or moist soils
log K_{ow}	2.95	LogKow of 3 indicates a potential for bioaccumulation under acid to neutral pH conditions
pKa	N/A	No dissociation observed
UV-visible absorption	Maximum absorbance at 218-272 nm	

Table 13 Table of Maximum Formation of Transformation Products

Code	Chemical name	Chemical structure	Study (duration, d)	Max %AR (day)
PARENT				
Momfluorothrin	2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (*EZ*)-(1*RS*,3*RS*;1*RS*,3*SR*)-3-(2-cyanoprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate			
MAJOR (>10%) TRANSFORMATION PRODUCTS				
MFOA			Aerobic aquatic – Water/ Sediment System (105-146-d)	35% (day 8)
			Hydrolysis (21-d)	96.2% (pH 9 at 50°C)
			Aqueous photolysis (13-d)	26.6%
MFOA-D			Aerobic soil (122-d)	76.8 (day 14)
			Aerobic aquatic – Water/ Sediment system (105-146-d)	72.9-74.5% (day 15-100)
			Hydrolysis (21-d)	96.2% (pH9, 50°C)
TFPA			Aerobic soil (122-d)	19.5% (day 63)
			Aerobic aquatic – Water/ Sediment system (105-146-d)	67.5% (day 105)
Z-CMCA			Aerobic soil (122-d)	53.0% (day 14)
			Hydrolysis (21-d)	94.1% (pH 9 at 40°C).
			Aerobic aquatic – Water/ Sediment System (105-146-d)	72 - 83.7% (day 8)
CMCA			Aerobic soil (122-d)	53% (day 14)
			Aqueous photolysis (13-d)	30.9 -38.8%
ωc-$CONH_2$-d-t-CRA			Aerobic soil	10.3% (day 30)
			Aerobic aquatic – Water/ Sediment System (105-146-d)	21% (day 100)
ωt-$CONH_2$-d-t-CRA			Aerobic soil (122-d)	16.4% (day 7)

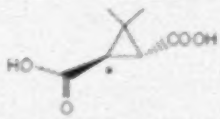
Code	Chemical name	Chemical structure	Study (duration, d)	Max %AR (day)
			Aerobic aquatic – Water/ Sediment System (105-146-d)	21 % (day 100)
ωt-COOH-d-t-CRA			Aerobic soil (122-d)	12.1% (day 7)
E-CMCA			Aerobic soil (122-d)	14.1% (day 3)
			Aerobic aquatic – Water/ Sediment System (105-146-d)	59.8 - 64.3% (day 7 -30)
t-COOH-CA			Aerobic soil (122-d)	11.9% (7)
			Aerobic aquatic – Water/ Sediment System (105-146-d)	10.3% (day 58)

Table 14 Fate and Behaviour in the Environment of Momfluorothrin

Property	Test substance	Value	Transformation products	Comments	Reference
Abiotic transformation					
Hydrolysis (21-d, pH 9 or 33-d, pH 7)	Momfluorothrin	pH 4: stable pH 7: 660-1394 days (20°C*), 381-723 days (25°C*) pH 9: 11.7-12.2 days (20°C*); 6.5 – 7.2 days (25°C) (*determined by extrapolation from higher temperatures)	MFOA and Z-CMCA	Hydrolysis occured at pH 9	2266957
Phototransformation in water (13-d; pH 4)	Momfluorothrin	$t_{1/2}$: 13 days continuous illumination (equivalent to 31.7 US solar days at 40°N latitude; 10.2 hours sunlight/day)	MFOA and CMCA	Transformation occurred in light at pH 4; stable in dark	2266953
Biotransformation					
Biotransformation in aerobic soil	Momfluorothrin	DT_{50} : 1.4 – 4.9 days DT_{90} : 8.7 – 25.6 days	MFOA-D, TFPA, Z-CMCA, CMCA, ωc-$CONH_2$-d-t-CRA, ωt-$CONH_2$-d-t-CRA, ωt-COOH-d-t-CRA, E-CMCA, t-COOH-CA	Non-persistent	2266949
Biotransformation in water/sediment systems	Momfluorothrin	DT_{50}: 0.1- 2.9 days DT_{90}:3.3 – 9.7 days	MFOA, MFOA-D, TFPA, Z-CMCA, CMCA, ωc-$CONH_2$-d-t-CRA , ωt-$CONH_2$-d-t-CRA, E-CMCA, t-COOH-CA	Non-persistent	2299069

Property	Test substance	Value	Transformation products	Comments	Reference
Mobility					
Adsorption / desorption in soil	Momfluorothrin	Adsorption: K_{ads}: 4.85 – 42.5 K_{oc}: 1033 - 4344 Desorption: K_{des}: 9.03 – 53.5 K_{oc}: 1085 – 6219	N/A	Low mobility	2299064
Stability in air (AOPWIN version 1.92a, USEPA)	Momfluorothrin	$t_{1/2}$< 0.455 days	N/A		2266912
Bioconcentration (bluegill sunfish)	Momfluorothrin	bioconcentration factor: 600-612	MFOA-D, TFPA	Unlikely to bioaccumulate	2266813

Table 15 Effects of Momfluorothrin on Non-Target Organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Reference
Non target terrestrial organisms					
Invertebrates					
Earthworm	14-d Acute	Momfluorothrin	15.6 mg a.i./kg dry soil	N/A	2266828
Bee	48-h Oral	Momfluorothrin	5.08 µg a.i./bee	Moderately toxic	2266830
	48-h Contact		0.20 µg a.i./bee	Highly toxic	
	Field weathered residue	X-6935-12	RT_{25} < 3 hours	N/A	2266801
Birds					
Bobwhite quail	Acute oral	Momfluorothrin	LD_{50} > 2250 mg a.i./kg bw	Practically non-toxic	2266831
	8-d Dietary	Momfluorothrin	LD_{50} > 1039 mg a.i./kg bw/day	Practically non-toxic	2266826
	20-week Reproduction	Momfluorothrin	NOEL < 19.6 mg a.i./kg bw/day	N/A	2266820
Mallard duck	8-d Dietary	Momfluorothrin	LD_{50} > 1935 mg a.i./kg bw/day	Practically non-toxic	2266827
	2-week Reproduction	Momfluorothrin	NOEL = 64.7 mg a.i./kg bw/day	N/A	2266819
Zebra finch	Acute oral	Momfluorothrin	LD_{50}>2250 mg a.i./kg bw	Practically non-toxic	2266829
Mammals					
Rat	Acute	Momfluorothrin	300 < LD_{50} < 2000 (♀) LD_{50} > 2000 (♂)	Practically non-toxic	2299086
	Multi generation-Reproduction	Momfluorothrin	NOEL = 32.1 mg a.i./kg bw/day	N/A	2266864
Vascular plants					
Vascular plants	Leaf and stem spraying of cabbage, tomato, cucumber and wheat at 500 g product/10 m^2	S-1563WBA (EP; 0.1% w/w Momfluorothrin)	Some growth suppression in tomato; partial necrosis in wheat	Qualitative	2266799 2266808
Non target aquatic organisms					
Freshwater species					
Daphnia magna	48-h Acute	Momfluorothrin	EC_{50}: 7.8µg a.i./L	Very highly toxic	2266825
	21-d Chronic	Momfluorothrin	NOEL: 3.1 µg a.i./L LOEL: 9.3 µg a.i./L	N/A	2266814
Rainbow trout	96-h Acute	Momfluorothrin	LC_{50} : 1.2 µg a.i./L	Very highly toxic	2266824
Bluegill sunfish	96-h Acute	Momfluorothrin	LC_{50}: 3.0 µg a.i./L	Very highly toxic	2266822
Fathead minnow	96-h Acute	Momfluorothrin	LC_{50}: 7.6 µg a.i./L	Very highly toxic	2266823
	ELS	Momfluorothrin	NOEC: 3.1 µg a.i./L	N/A	2266818

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Reference
Freshwater alga *Pseudokirchneriella subcapitata*	96-h Acute	Momfluorothrin	IC_{50}: N/A[b] NOEC: 0.37 mg a.i./L	N/A	2266821
Vascular plant *Lemna gibba*	7-d dissolved	Momfluorothrin	IC_{50} > 2.5 mg a.i./L	N/A	2266815
Midge larvae *Chironomus dilutus*	49-d chronic	Momfluorothrin	EC_{50}: 0.14 mg ai/kg sediment NOEC[c] < 0.013 mg a.i./kg sediment	N/A	2266817

a: Atkins *et al.*(1981) for bees and USEPA classification for others, where applicable
N/A: Not applicable
b: The IC_{50} could not be determined due to study deficiencies
c: NOEC could not be determined

Table 16 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints
Toxic or toxic equivalent as defined by the *Canadian Environmental Protection Act* [1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	Half-life < 5 days
	Water	Half-life ≥ 182 days	Half-life < 3 days
	Sediment	Half-life ≥ 365 days	Half-life unknown
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life 3.1 days Volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (2.5×10^{-7} Pa at 20°C) and Henry's Law Constant (1.025x10-4 Pa m^3/mol).
Bioaccumulation[4]	Log K_{OW} ≥ 5		2.95
	bioconcentration factor ≥ 5000		bioconcentration factor = 600-612
	bioaccumulation factor ≥ 5000		Value or not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.

1 All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (in other words, all other TSMP criteria are met).

2 The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

3 If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) then the criterion for persistence is considered to be met.

4 Field data (for example, bioaccumulation factors) are preferred over laboratory data (for example, bioconcentration factors) which, in turn, are preferred over chemical properties (for example, log K_{OW}).

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
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2266908	2012, S-1563PAI: Calculations of Henry's Law Constant, DACO: 2.14.9
2266909	2012, S-1563 TGAI: Determination of Physical State, Colour and Odour, DACO: 2.14.1,2.14.2,2.14.3
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2266911	2012, S-1563TGAI: Determination of Relative Density, DACO: 2.14.6
2266914	2011, S-1563RTE: Determination of Octanol: water partition coefficient, DACO: 2.14.11
2266916	2011, S-1563RTZ: Determination of Octanol: water partition coefficient, DACO: 2.14.11
2266920	2011, S-1563RTZ: Evaluation of Dissociation Constant, DACO: 2.14.10
2266921	2011, S-1563TGAI: Determination of Solvent Solubility, DACO: 2.14.8
2266922	2011, S-1563 TGAI: Determination of pH, DACO: 2.16
2266923	2011, S-1563RTZ: Determination of Melting/Boiling Point, DACO: 2.14.4,2.14.5
2266924	2011, S-1563RTE: Determination of Melting/Boiling Point, DACO: 2.14.4,2.14.5
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2266929	2010, S-1563RTZ: Evaluation of Vapour Pressure, DACO: 2.14.9
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2266970	2011, Enforcement Analytical Methods of S-1563 Technical Material, DACO: 2.13.1 CBI
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2299051	2012, Description of Materials Used to Produce S-1563; Description of Production Process of S-1563; Description of Formulation Impurities of S-1563, DACO: 2.11.1,2.11.2,2.11.3,2.11.4 CBI
2299052	2012, Product Identity and Disclosure of Ingredients of S-1563 Technical Grade, DACO: 2.12.1,2.4,2.5 CBI
2299054	2012, Certification of Ingredient Limits of S-1563 Technical Grade, DACO: 2.12.1 CBI
2299055	2011, Long-Term Stability of S-1563, DACO: 2.14.14 CBI
2299056	2011, Preliminary Analysis of S-1563 Technical Material, DACO: 2.13 CBI
2299057	2011, Enforcement Analytical Methods of S-1563 Technical Material, DACO: 2.13.1 CBI
2299075	2013, Active Substance: S-1563; Insecticide Products: S-1563 MUP & S-1563 WBA, DACO: 2.11.2,2.11.3,2.11.4,2.12.1,2.13.1,2.13.2,2.13.3 CBI
2299077	2013, IIA2 Identity of the Active Substance, DACO: 2.11.1,2.12.1,2.4,2.5
2317115	2013, Discussion of Formation of Impurities, DACO: 2.11.4
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2319649	2013, Physical and Chemical Properties of the Active Substance, DACO: 2.14.1,2.14.10,2.14.11,2.14.12,2.14.13,2.14.14,2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.7,2.14.8,2.14.9,2.16
2266973	2011, Development and Validation of a Analytical Method for the Determination of S-1563 in Soil, DACO: 8.2.2.1

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2319650	2012, Description of Methods for Analysis of Soil, DACO: 8.2.2.1
2266646	2012, S-1563MUP: Determination of Relative Density, DACO: 3.5.6
2266647	2012, S-1563MUP: Determination of pH, DACO: 3.5.7
2266648	2012, Waiver Request for Group B Product Properties for S-1563MUP, DACO: 3.5.13,3.5.8
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2299122	2012, Certification of Ingredient Limits of S-1563 Manufacturing Use Product, DACO: 3.3.1 CBI
2299123	2012, S-1563 MUP: Assessment of Explosive Properties, DACO: 3.5.12 CBI
2299124	2012, Enforcement Analytical Methods of S-1563 MUP, DACO: 3.4.1 CBI
2299126	2013, IIIA1 Identity of the Manufacturing Use Product (MUP), DACO: 3.2.1,3.3.1
2304765	2013, Document J - RWF 0048, DACO: 3.3.1 CBI
2304766	2012, Description of Analytical Methods for the Determination of the Active Substance in Plant Protection Products - RWA-0025, DACO: 3.4.1
2319606	2013, Identity of the Biocidal Product (MUP), DACO: 3.1,3.2.1,3.3.1
2319607	2012, Description of Analytical Methods For The Determination of the Active Substance in Plant Protection Products, DACO: 3.4.1
2266764	2012, S-1563/Sumithrin WBA(USA): Determination of Physical State, Colour and Odour, DACO: 3.5.1,3.5.2,3.5.3
2266765	2012, IIIA2 Phys Chem Product, DACO: 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.8, 3.5.9, 3.7 CBI
2266769	2013, Formulation Type, DACO: 3.5.4
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2266772	2012, Aerosol Flammability Testing and Internal Pressure Measurement on a Sample of S-1563/Sumithrin WBA (USA), DACO: 3.5.11
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2266779	2013, S-1563 EP Corrosion Characteristics schedule, DACO: 3.5.14
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2299104	2012, Product Identity and Disclosure of Ingredients of S-1563 Flying and Crawling Insect Killer Spray, DACO: 3.2.1,3.3.1 CBI
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2299108	2012, S-1563/Sumithrin WBA (USA): Determination of Viscosity, DACO: 3.5.9
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2267096	2012, Formulation Process Description for MGK 2983, DACO: 3.2.1, 3.2.2, 3.2.3, 3.3.1 CBI
2267097	2012, Product Chemistry of MGK 2983, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI

2267098	2012, 3.5.4-3.5.5, DACO: 3.5.4,3.5.5 CBI
2316537	2013, Product Chemistry of MGK 2981, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2317421	2013, Product Chemistry of MGK 2983, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2326589	2013, Product Chemistry of MGK 2983, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2386775	2013, Storage Stability Evaluation of MGK 2983, DACO: 3.5.10,3.5.14 CBI
2267463	2012, 3.1.1-3.1.4, DACO: 3.1.1,3.1.2,3.1.3,3.1.4 CBI
2267464	2012, Formulation Process Description for MGK® 29831, DACO: 3.2.1,3.2.2,3.2.3,3.3.1 CBI
2267466	2012, Product Chemistry of MGK 29831, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2267467	2012, 3.5.4-3.5.5, DACO: 3.5.4,3.5.5 CBI
2316491	2013, Product Chemistry of MGK 29831, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2317405	2013, Product Chemistry of MGK 29831, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2326636	2013, Product Chemistry of MGK 29831, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2386811	2013, Storage Stability of MGK 29831, DACO: 3.5.10,3.5.14 CBI
2267148	2012, 3.1.1-3.1.4, DACO: 3.1.1,3.1.2,3.1.3,3.1.4 CBI
2267149	2012, Formulation Process Description for MGK 2987, DACO: 3.2.1, 3.2.2, 3.2.3, 3.3.1 CBI
2267151	2012, Product Chemistry of MGK 2987, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2267152	2012, 3.5.4-3.5.5, DACO: 3.5.4,3.5.5 CBI
2316541	2013, Product Chemistry of MGK 2987, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI

2317426	2013, Product Chemistry of MGK 2987, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2317427	2013, Product Chemistry of MGK 2987, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2326593	2013, Product Chemistry of MGK 2987, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2386771	2013, Storage Stability Evaluation of MGK 2987, DACO: 3.5.10,3.5.14 CBI
2267690	2012, 3.1.1-3.1.4, DACO: 3.1.1,3.1.2,3.1.3,3.1.4 CBI
2267692	2012, Formulation Process Description for MGK ® 29871, DACO: 3.2.1, 3.2.2, 3.2.3, 3.3.1 CBI
2267693	2012, Product Chemistry of MGK 29871, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2267695	2012, 3.5.4-3.5.5, DACO: 3.5.4,3.5.5 CBI
2316525	2013, Product Chemistry of MGK 29871, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2317416	2013, Product Chemistry of MGK 29871, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2326659	2013, Product Chemistry of MGK 29871, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2386803	2013, Storage Stability Evaluation of MGK 29871, DACO: 3.5.10,3.5.14 CBI
2267578	2012, 3.1.1-3.1.4, DACO: 3.1.1,3.1.2,3.1.3,3.1.4 CBI
2267579	2012, Formulation Process Description for MGK ® 29872, DACO: 3.2.1, 3.2.2, 3.2.3, 3.3.1 CBI
2267582	2012, Product Chemistry of MGK 29872, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2267585	2012, 3.5.4-3.5.5, DACO: 3.5.4,3.5.5 CBI
2316506	2013, Product Chemistry of MGK 29872, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI

2317407	2013, Product Chemistry of MGK 29871, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2326645	2013, Product Chemistry of MGK 29872, DACO: 3.2.3, 3.4.1, 3.4.2, 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8,3.5.9 CBI
2386788	2013, Storage Stability Evaluation of MGK 29872, DACO: 3.5.10,3.5.14 CBI
2435109	2012, Determination of Dielectric Breakdown Voltage for MGK 29872, DACO: 3.5.15 CBI
2437955	2014, pH Determination of MGK 29872, DACO: 3.5.7 CBI

2.0 Human and Animal Health

PMRA Document Number	Reference
2266651	2012, Acute Oral Toxicity Study of S-1563MUP in Rats, DACO: 4.2.1
2266653	2012, Acute Dermal Toxicity Study of S-1563MUP in Rats, DACO: 4.2.2
2266655	2012, Acute Inhalation Toxicity Study of S-1563 in Rats, DACO: 4.2.3
2266656	2012, Acute Inhalation Toxicity Study of S-1563 MUP in Albino Rats, DACO: 4.2.3
2266659	2012, An Eye Irritation Study of S-1563MUP in Rabbits, DACO: 4.2.4
2266661	2012, A Skin Irritation Study of S-1563MUP in Rabbits, DACO: 4.2.5
2266663	2012, A Skin Sensitization Study of S-1563MUP in Guinea Pigs (Buehler Test), DACO: 4.2.6
2266780	2012, Acute Oral Toxicity Study of S-1563/Sumithrin WBA (USA) Bulk Formulation in Rats, DACO: 4.6.1
2266782	2012, Acute Dermal Toxicity Study of S-1563/Sumithrin WBA (USA) Bulk Formulation in Rats, DACO: 4.6.2
2266784	2012, S-1563/Sumithrin WBA(USA): Toxicity Study by Inhalation Administration to Rats for 1 Week, DACO: 4.6.3
2266788	2012, An Eye Irritation Study of S-1563/Sumithrin WBA(USA) Bulk Formulation in Rabbits, DACO: 4.6.4
2266790	2012, A Skin Irritation Study of S-1563/Sumithrin WBA(USA) Bulk Formulation in Rabbits, DACO: 4.6.5
2266792	2012, A Skin Sensitization Study of S-1563/Sumithrin WBA(USA) Bulk Formulation in Guinea Pigs (Buehler Test), DACO: 4.6.6

2266832	2012, An Evaluation of the Human Relevance of S-1563-Induced Liver Tumours in Rats Based on Mode of Action, DACO: 4.8
2266833	2012, Study for the Mode of Action Analysis for Tumour Formation of S-1563 in Rat Liver (6): - In vitro Evaluation for Role of Nuclear Receptor CAR in S-1563 - and Its Metabolite Z-CMCA-induced CYP2B1/2 mRNA Expression of Cultured Rat Hepatocytes, DACO: 4.8
2266847	2012, Study for Mode of Action Analysis for Effects of S-1563 on Thyroid Gland in Male Rats, DACO: 4.8
2266848	2012, Study for Mode of Action Analysis for Tumour Formulation of S-1563 on Rat Liver (5) - Analysis for Time Course and Dose Response in Female Rats, DACO: 4.8
2266849	2012, Study for Mode of Action Analysis for Tumour Formulation of S-1563 on Rat Liver (4) - The 2nd Study for Dose Response Analysis in Male Rats, DACO: 4.8
2266850	2012, Study for Mode of Action Analysis for Tumour Formulation of S-1563 on Rat Liver (3) - Time Course Analysis at High Dose of S-1563 in Male Rats, DACO: 4.8
2266851	2012, Study for Mode of Action Analysis for Tumour Formulation of S-1563 on Rat Liver (2) - Analysis for Time Course, Dose Response and Reversibility in Male Rats, DACO: 4.8
2266852	2012, Study for Mode of Action Analysis for Tumour Formulation of S-1563 on Rat Liver (1) - Time Course Analysis in Male Rats, DACO: 4.8
2266853	2012, Study for Mode of Action Analysis for Effects of S-1563 on Female Mouse Liver - Time Course, Dose Response and Reversibility, DACO: 4.8
2266854	2012, Study for Mode of Action Analysis for Effects of S-1563 on Male Mouse Liver - Dose Response and Reversibility, DACO: 4.8
2266855	2012, Study for Mode of Action Analysis for Effects of S-1563 on Male Mouse Liver - Time course Analysis, DACO: 4.8
2266856	2012, S-1563: 104 Week Oncogenicity (Feeding) Study in the Wistar Rat, DACO: 4.4.3
2266862	2012, Vol. 1 of 2 (Text, Figures, Summary Tables and Appendices A-H) S-1563 A 28-Day Oral (Dietary) Immunotoxicity Study in Male Wistar Han Rats, DACO: 4.8
2266863	2012, A 28-Day Repeated Dose Dermal Toxicity Study of S-1563 in Rats, DACO: 4.3.5
2266864	2012, S-1563: Two-Generation Reproduction Toxicity Study in the Han Wister Rat, DACO: 4.5.1
2266865	2012, S-1563: 78-Week Oncogenicity (Feeding) Study in the CD-1 Mouse, DACO: 4.4.2

2266866	2012, Dose Range-Finding Study for Acute Neurotoxicity Study in Rats, DACO: 4.5.12,4.5.13
2266875	2011, Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro (V79/HPRT) with S-1563, DACO: 4.5.5
2267100	2012, Acute Oral Toxicity Up And Down Procedure In Rats, DACO: 4.6.1
2267102	2012, Acute Dermal Toxicity Study in Rats- Limit Test, DACO: 4.6.2
2267103	2012, Acute Inhalation Toxicity Study in Rats-Limit Test, DACO: 4.6.3
2267105	2012, Primary Eye Irritation Study in Rabbits, DACO: 4.6.4
2267106	2012, Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
2267107	2012, Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6
2267153	2012, Acute Oral Toxicity Up And Down Procedure In Rats, DACO: 4.6.1
2267154	2012, Acute Dermal Toxicity Study in Rats- Limit Test, DACO: 4.6.2
2267155	2012, Acute Inhalation Toxicity Study in Rats-Limit Test, DACO: 4.6.3
2267157	2012, Primary Eye Irritation Study in Rabbits, DACO: 4.6.4
2267159	2012, Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
2267161	2012, Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6
2267469	2012, Acute Oral Toxicity Up And Down Procedure In Rats, DACO: 4.6.1
2267470	2012, Acute Dermal Toxicity Study in Rats- Limit Test, DACO: 4.6.2
2267471	2012, Acute Inhalation Toxicity Study in Rats-Limit Test, DACO: 4.6.3
2267472	2012, Primary Eye Irritation Study in Rabbits, DACO: 4.6.4
2267473	2012, Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
2267475	2012, Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6
2267587	2012, Acute Oral Toxicity Up And Down Procedure In Rats, DACO: 4.6.1
2267589	2012, Acute Dermal Toxicity Study in Rats- Limit Test, DACO: 4.6.2
2267590	2012, Acute Inhalation Toxicity Study in Rats-Limit Test, DACO: 4.6.3
2267592	2012, Primary Eye Irritation Study in Rabbits, DACO: 4.6.4
2267596	2012, Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
2267597	2012, Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6
2267697	2012, Acute Oral Toxicity Up And Down Procedure In Rats, DACO: 4.6.1
2267698	2012, Acute Dermal Toxicity Study in Rats- Limit Test, DACO: 4.6.2
2267699	2012, Acute Inhalation Toxicity Study in Rats-Limit Test, DACO: 4.6.3

2267700	2012, Primary Eye Irritation Study in Rabbits, DACO: 4.6.4
2267701	2012, Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
2267702	2012, Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6
2299062	2011, 13-Week Repeated Dose Oral (Capsule) Toxicity Study in the Beagle Dog Followed by a 6-Week Recovery Period, DACO: 4.3.8
2299063	2012, S-1563: 52-Week Chronic Toxicity (Feeding) Study in the Wistar Rat, DACO: 4.4.1
2299070	2011, Study for Effects on Embryo-Fetal Development of S-1563 Administered Orally to Rabbits, DACO: 4.5.3
2299072	2011, S-1563: 13-Week Neurotoxicity (Feeding) Study in Rats, DACO: 4.5.12,4.5.13
2299073	2012, S-1563: Acute Oral Neurotoxicity Study in Rats, DACO: 4.5.12,4.5.13
2299074	2012, Letter of Authorization Developmental Neurotoxicity, DACO: 4.5.14
2299078	2009, Reverse Mutation Test of S-1563 in Bacterial Systems, DACO: 4.5.4
2299080	2013, Two Generation Reproductive Toxicity in the Rat, DACO: 4.5.1
2299081	2009, Metabolism of S-1563RTZ in Rats - Distribution, Metabolism and Excretion in Rats after Repeated Oral Administration, DACO: 4.5.9
2299082	2011, The Disposition and Metabolism of S-1563RTZ and S-1563RTE in Rats (a single administration), DACO: 4.5.9
2299084	2009, In vitro Chromosomal Aberration Test on S-1563 in Chinese Hamster Lung Cells (CHL/IU), DACO: 4.5.6
2299085	2010, Micronucleus Test on S-1563 in Rats, DACO: 4.5.7
2299086	2011, Acute Oral Toxicity Study of S-1563 in Rats, DACO: 4.2.1
2299087	2010, Skin Sensitization Test of S-1563 in Guinea Pigs (Maximization Test), DACO: 4.2.6
2299088	2010, In Vivo Unscheduled DNA Synthesis (UDS) Assay with S-1563 in Rat Hepatocytes, DACO: 4.5.8
2299089	2011, Eye Irritation Test of S-1563 in Rabbits, DACO: 4.2.4
2299090	2011, Skin Irritation Test of S-1563 in Rabbits, DACO: 4.2.5
2299091	2010, Acute Dermal Toxicity Study of S-1563 in Rats, DACO: 4.2.2
2299092	2011, Study on the Effect of Oral Administration of S-1563 on Embryo-Fetal Development in Rats, DACO: 4.5.2
2299093	2011, Acute Inhalation Toxicity Study of S-1563 in Rats, DACO: 4.2.3
2299094	2011, Four-Week Repeated Inhalation Toxicity Study of S-1563 in Rats, DACO: 4.3.7

2324610	2010, Skin Sensitization Test of S-1563 in Guinea Pigs (Maximization Test) Amended Report to Replace MRID # 490200-04, DACO: 4.2.6
2324611	2011, 13-Week Repeated Dose Oral (Feeding) Toxicity Study in the Wistar Rat Followed by a 6-Week Recovery Period (Amended Report to Replace MRID # 490200-06, DACO: 4.3.1

3.0 Environment

PMRA Document Number	Reference
2266808	2012, Waiver Request from Further Testing: Non-Target Terrestrial Plant Testing; Seedling Emergence and Vegetative Vigor, DACO: 9.9
2266809	2012, Waiver Request from Further Testing: Whole Sediment Acute or Chronic Toxicity Testing with Marine Organisms, DACO: 9.9
2266810	2012, Waiver Request from Further Testing: Chronic Toxicity Testing with Estuarine and Marine Organisms, DACO: 9.9
2266811	2012, Waiver request from Further Testing: Estuarine and Marine Organism Acute Toxicity Testing, DACO: 9.9
2266812	2012, Waiver Request from Further Testing: Non-Target Plant Toxicity Testing with Three Algal Species, DACO: 9.9
2266813	2012, Flow-Through Bioconcentration and Metabolism Study of [^{14}C]S-1563 with Bluegill Sunfish (*Lepomis macrochirus*), DACO: 9.5.6
2266814	2012, S-1563 - Full Life Cycle Toxicity Test with Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Following OPPTS Draft Guideline 850.1300, OECD Guideline #211 and The Official Journal of the European Communities L383A, Method C.20, DACO: 9.3.3
2266815	2012, S-1563 - 7 Day Toxicity Test with Duckweed (*Lemna gibba*), DACO: 9.8.5
2266817	2012, S-1563 - Toxicity Test with Sediment-Dwelling Midges (*Chironomus dilutes*) Under Static Conditions, Following OECD Guideline 218, DACO: 9.9
2266818	2012, S-1563 - Early Life-Stage Toxicity Test with Fathead Minnow, *Pimephales promelas*, Following OECD Guideline #210 and OPPTS Draft Guideline 850.1400, DACO: 9.5.3.1
2266819	2012, S-1563: A Reproduction Study with the Mallard, DACO: 9.6.3.2
2266820	2012, S-1563: A Reproduction Study with the Northern Bobwhite, DACO: 9.6.3.1
2266821	2011, S-1563 - 96-Hour Toxicity Test with the Freshwater Green Alga, *Pseudokirchneriella subcapitata*, Following OPPTS Draft Guideline 850.5400, the Official Journal of the European Union Commission Regulation (EC) No 761/2009 Annex IV Method C.3 and OECD Guideline #201, DACO: 9.8.2
2266823	2011, S-1563 - Acute Toxicity to Fathead Minnow (*Pimephales promelas*) Under Flow-Through Conditions, Following OPPTS Draft Guideline 850.1075, OECD Guideline #203 and The Official Journal of the European Communities L383A, Method C.1, DACO: 9.5.2.3

2266824	2011, S-1563 - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions, Following OPPTS Draft Guideline 850.1075, OECD Guideline #203 and The Official Journal of the European Communities L383A, Method C.1, DACO: 9.5.2.1
2266825	2011, S-1563 - Acute Toxicity to Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Following OECD Guideline #202, OPPTS Draft Guideline 850.1010 and The Official Journal of the European Community L383A, Method C.2, DACO: 9.3.2
2266826	2011, S-1563: A Dietary LC50 Study with the Northern Bobwhite, DACO: 9.6.2.4
2266827	2011, S-1563: A Dietary LC50 Study with the Mallard, DACO: 9.6.2.5
2266828	2010, Acute Toxicity of S-1563 on Earth Worms, *Eisenia fetida* using an artifical soil test, DACO: 9.2.3.1
2266829	2010, S-1563: An Acute Oral Toxicity Study with Zebra Finch (*Poephila guttata*), DACO: 9.6.2.3
2266830	2010, Acute Oral and Contact Toxicity to the Honeybee *Apis Mellifera*, L. in the Laboratory, DACO: 9.2.4.1, 9.2.4.2
2266831	2010, S-1563: An Acute Oral Toxicity Study with the Northern Bobwhite, DACO: 9.6.2.1
2299086	2011, Acute Oral Toxicity Study of S-1563 in Rats, DACO: 4.2.1
2266864	2012, S-1563: Two-Generation Reproduction Toxicity Study in the Han Wistar Rat, DACO: 4.5.1
2266912	2011, Stability of S-1563 in Air (Calculation by Atkinson's Method), DACO: 8.2.3.3.3
2266945	2012, Waiver Request from Further Testing: Terrestrial Field Dissipation, DACO: 8.6
2299064	2012, Soil Absorption/Desorption of [^{14}C]S-1563 by the Batch Equilibrium Method, DACO: 8.2.4.2
2266949	2012, Aerobic Soil Metabolism of [^{14}C]S-1563 in Four Soils, DACO: 8.2.3.4.2
2266953	2012, Photodegradation of [^{14}C]S-1563 in Aqueous Solutions Buffered by pH 4 by Artificial Light, DACO: 8.2.3.3.2
2266957	2011, Hydrolysis of [^{14}C]S-1563 in Buffered Aqueous Solutions, DACO: 8.2.3.2
2299069	2011, [^{14}C]S-1563: Degradation in Water Sediment Systems under Aerobic Conditions, DACO: 8.2.3.5.4
2266963	2011, Estimation of the Adsorption Coefficient (Koc) of S-1563 RTZ and S-1563 RTE using High Performance Liquid Chromatography, DACO: 8.2.3.5.4
2266801	2012, X-6935-12: Residual Toxicity to the Honey Bee (*Apis mellifera* L.) under Extended Laboratory Conditions when applied as a Foliar Spray to Alfalfa Leaves, DACO: 8.2.3.5.4

4.0 Value

PMRA Document Number	Reference
2266736	2012, Laboratory bioassay to determine the efficacy of aerosol products against mosquitoes, *Aedes albopicutus*, bed bugs, *Cimex lectularius* and black ants, *Lasius niger*, applied as direct spray, DACO: 10.2.3.2
2266738	2012, Evaluation of a Spray Containing S-1563 (Water Based Aerosol) For Knockdown and Kill of Caged Flies and Mosquitoes, DACO: 10.2.3.2
2266739	2012, Evaluation of a Spray Containing S-1563 (Water Based Aerosol) For Knockdown and Kill of Crawling Venomous Arthropods (Scorpions, Spiders and Centipedes), DACO: 10.2.3.2
2266749	2012, Evaluation of a Spray Containing S-1563 (Water Based Aerosol) For Knockdown and Kill of Caged Stinging Hymenopterans (Yellow Jackets, Hornets, and Paper Wasps), DACO: 10.2.3.2
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2266752	2012, Evaluation of Sum and Sum/S-1563 (WBA) as Fast-Acting Space Sprays Against Flying Insects in a 6x6x6 Foot Peet Grady Chamber, DACO: 10.2.3.2
2266967	2011, Characteristic of Insecticidal Activity of S-1563 Technical Grade, DACO: 10.2.3.2
2317096	2013, Value Summary, DACO: 10.1
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2317105	2013, Efficacy: Laboratory, Growth Chamber Trial, DACO: 10.2.3.2
2319586	2012, Active Substance: S-1563 Product: 0.1% S-1563 + 0.2% Sumithrin (d-phenothrin) Water Based Aerosol Efficacy Data and Information, DACO: 10.2.3.2
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2267454	2012, Efficacy Evaluations of Four (4) Aerosol Formulations to Determine Contact Activity (knock down & mortality) Against Pyrethroid Resistant and Susceptible House Flies, *Musca domestica*, in the Laboratory Bioassay, DACO: 10.2.3.2(C)
2316484	2009, Laboratory trial to evaluate S-1563 for efficacy against German cockroaches, *Blattella germanica*, bed bugs, *Cimex lectularius*, dog ticks, *Rhipicephalus sanguineus*, litter beetles, *Alphitobius diaperinus*, and houseflies, *Musca domestica*, DACO: 10.1,10.2.3.2

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2267674	2012, Efficacy of MGK 29871 (0.20% Sumithrin, 0.05% S-1563) and 29872 (0.20% Sumithrin, 0.05% S- 1563) Aerosol Formulations When Applied as Direct Spray Applications against Paper Wasps (*Polistes* spp), DACO: 10.2.3.2(C)
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2316512	2009, Laboratory trial to evaluate 8-1563 for efficacy against German cockroaches, *Blattella germanica*, bed bugs, *Cimex lectularius*, dog ticks, *Rhipicephalus sanguineus*, litter beetles, *Alphitobius diaperinus*, and houseflies, *Musca domestica*, DACO: 10.1,10.2.3.2(A)

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

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